Insulin and Glucose Responses to Various Starch-Containing Foods in Type II Diabetic Subjects

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The circulating insulin and glucose responses in type II diabetic subjects were determined for 5 h after ingestion of various meals, each containing 50 g carbohydrate. The purpose of the study was to *1*) systematically study the insulin response to several different high-starch foods, *2*) determine whether this insulin response could be predicted by the glucose response, and *3*) determine whether the glucose response could be predicted by the physical structure and digestibility of the ingested carbohydrate. Each subject served as his own control. Carbohydrate was given in the form of potatoes, bread, oatmeal, rice, lentils, kidney beans, cornflakes, high-amylose corn muffins, and low-amylose corn muffins. Bread, oatmeal, rice, lentils, kidney beans, and high-amylose corn muffins resulted in a significantly lower glucose area than 50 g glucose, and the glucose response generally could be predicted by the physical structure and the known digestibility of the ingested carbohydrate. The insulin rise was statistically significantly greater than would be predicted from the glucose response for oatmeal, lentils, kidney beans, and high-amylose corn muffins. Although not statistically significant, the mean was greater than predicted for every other food except potatoes when the insulin response to 50 g glucose was used as a standard. These results indicate that the insulin response cannot be predicted by the glucose response. *Diabetes Care* 10:205–12, 1987

For the past several years we have been interested in the metabolic response to meals of varying composition (1–4). More recently, we have become particularly interested in determining the insulin response as well as the glucose response for various foods in untreated non-insulin-dependent (type II) diabetics. This was prompted by our observations that a mixed meal resulted in a much larger insulin response than that observed with a similar amount of CHO given as glucose alone (F.Q.N. and M.C.G., unpublished observations). The greater insulin secretion could partly be explained by the animal protein present in the mixed meal. However, based on data we had obtained previously, it could not entirely explain the difference (5). Therefore, we considered it necessary to determine if different representative high-CHO foods given individually as a single meal also stimulated a rise in circulating insulin concentration that was different for each food and that could not be explained by the plasma glucose response. Jenkins and associates (6) have suggested that in normal subjects the postmeal insulin response can be predicted by the postmeal glucose response.

In our studies we used untreated mild to moderately severe diabetic subjects, i.e., diabetic subjects who are most likely to be candidates for dietary management alone. Each subject served as his own control. In addition, the subjects were studied for 5 h after each meal because we previously had observed that this was the mean time required for the plasma glucose concentration to return to the fasting value after a meal with 50 g glucose. In addition, serum insulin returns to the baseline more slowly than plasma glucose. Analyzing data for only 3 h will considerably underestimate the serum insulin response to a meal. In previous studies by others, results were obtained only for 2–3 h (7–10). We present the results observed after ingestion of several commonly used high-starch foods. The response to a high-amylose and low-amylose cooked cornstarch was also studied.

MATERIALS AND METHODS

Study 1. Eight male untreated diabetic subjects were studied in a metabolic unit. All patients met the National Diabetes Data Group criteria for the diagnosis of type II diabetes mel-

litus (11). Mean age was 65 ± 2 yr (range 60–73 yr). Mean percent of desirable body weight according to the 1959 Metropolitan Life Insurance Tables for medium frames was 142 ± 9% (range 100–175%). All subjects signed an informed consent, and the study was approved by the Medical Center Committee on Human Subjects. All subjects were on diets containing at least 200 g CHO/day with adequate food energy for 3 days before testing. None of the subjects had been treated with oral hypoglycemic agents or insulin previously. This was done to avoid any potential confounding effects on endogenous insulin secretion.

After an overnight fast of 10–14 h, an indwelling catheter was inserted into an antecubital vein and kept patent with small amounts of heparin. The subjects were then given, in random order, a meal of 50 g CHO as estimated from food tables (12,13) in the form of glucose, lentils, kidney beans, potatoes, whole-wheat bread, rolled oatmeal, or parboiled long-grain enriched Uncle Ben's converted white rice. Protein and fat contents per 50 g CHO are presented in Table 1.

The glucose was given as 50 g of a standard glucose solution. All foods were prepared in individual portions and all cooking water was served with the food. The white rice was simmered in 150 ml of boiling water for 10 min. The potatoes were peeled, sliced, and cooked in a microwave at full power for 2.5–3 min until tender. The bread was 100% whole wheat served without butter or margarine. The oatmeal was boiled for 1 min then simmered for 5 min. The lentils were heated to boiling, covered, and simmered for 20 min, stored in a refrigerator, and warmed in a microwave before serving. The kidney beans were boiled for 2 min, soaked for 60 min, reheated to boiling, and simmered for 60 min. They were reheated before serving in a microwave oven. Up to 2 cups of water or decaffeinated coffee were given with each meal.

Study 2. A separate group of nine male untreated subjects, also fulfilling the National Diabetes Data Group Criteria for the diagnosis of type II diabetes mellitus (11), were studied with the same protocol except that the subjects ingested corn products of various amylose content. Mean age was 63 ± 2 yr (range 54–69 yr). Mean percent of desirable body weight according to the 1959 Metropolitan Life Insurance Tables for medium frames was 124 ± 9% (range 100–175%).

TABLE 1
Protein and fat content per 50 g CHO in starch meals

	Protein (g)	Fat (g)	Raw wt (g)	Dietary fiber (g)	Calories
Kidney beans	24.5	1.8	111	27.7	302
Lentils	22.4	0.9	94	11.0	286
Potato	5.0	0.2	240	5.0	209
Bread	10.6	3.2	120	10.2	259
Oatmeal	8.5	6.0	69	4.8	277
Rice	3.8	0.6	58	1.4	209
High amylose	6.9	29.1	166	0	502
Low amylose	6.9	29.1	166	0	502
Cornflakes	5.0	0.9	59	0.6	217

*Estimated from food tables in refs. 13 and 14.

TABLE 2
5-h glucose excretion (g)

	Mean ± SE	Range
Study 1		
Glucose	7.3 ± 3.0	0.1–26.4
Bread	6.4 ± 3.3	0.0–26.4
Potato	3.3 ± 1.7*	0.0–14.2
Oatmeal	4.3 ± 2.4*	0.1–20.0
Rice	3.4 ± 2.1*	0.1–18.1
Kidney beans	2.1 ± 1.1*	0.0–6.8
Lentils	1.4 ± 0.8*	0.0–6.1
Study 2		
Glucose	8.1 ± 4.1	0.0–35.3
High amylose	3.1 ± 1.9	0.0–16.4
Low amylose	4.8 ± 2.2	0.0–16.2
Cornflakes	5.2 ± 2.5	0.0–18.9

*Mean statistically significantly different from mean glucose meal results.

The corn products served were two types of cornstarch made into muffins: one with cornstarch with a high amylose content (65–75%, Amylomaize VII) and one with cornstarch with a low amylose content (0–7%, Waxy-Amioca). The cornstarches were a gracious gift from American Maize Products, Hammond, IN. The glucose and insulin responses to 50 g of these cornstarches were compared with those of commercial cornflakes with an amylose content of 25–30% and to 50 g of a standard glucose solution. The protein and fat content of the meals is given in Table 1. The cornstarch muffins were made by adding the cornstarch to a small amount of egg, buttermilk, and butter. They were then baked in a conventional oven and warmed in a microwave before serving. The cornflakes were served with water. Some patients poured the water over the cornflakes, while others preferred to eat the dry cornflakes and drink the water.

For both studies, blood was drawn for glucose and insulin measurements at 0, 0.5, 1, 2, 3, 4, and 5 h after ingestion of the test meal. Plasma glucose was determined by a glucose oxidase method with a Beckman glucose analyzer (Fullerton, CA). Serum immunoreactive insulin was measured by a standard double-antibody radioimmunoassay method with commercial kits purchased from Endotech (Louisville, KY).

Areas above the fasting baseline were determined by planimetry. Areas below the baseline were subtracted from areas above the baseline to give a net area. Calculating the net area occasionally results in a negative number; although this is certainly acceptable physiologically, it makes statistical analysis of the data difficult. To circumvent this difficulty, we have expressed some data as "predicted" vs. "observed" insulin values, based on the following relationship. The glucose response to a test meal is to the insulin response to a

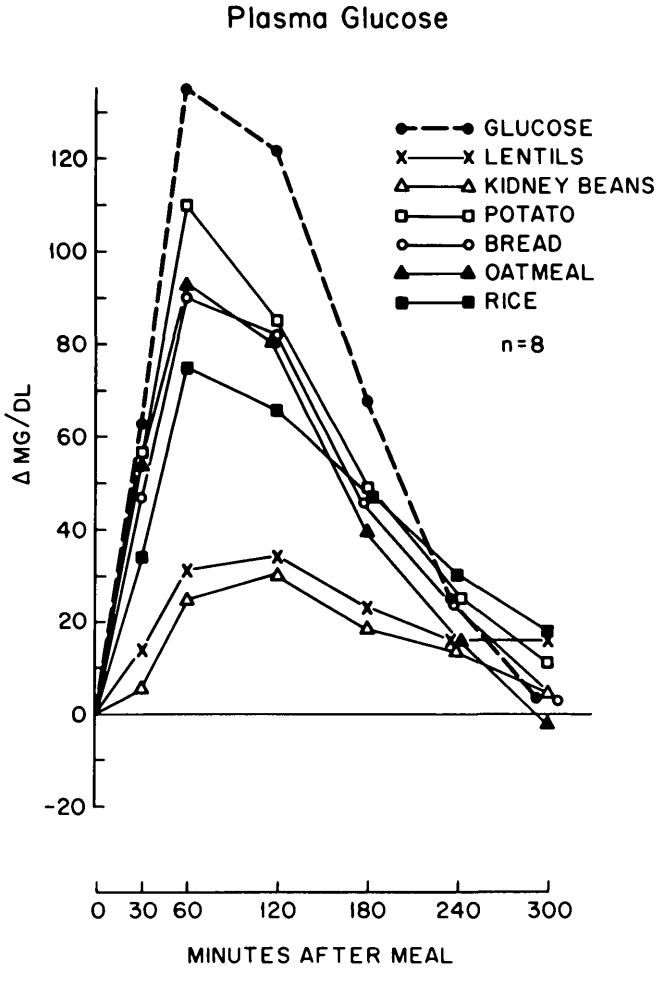

FIG. 1. Plasma glucose response to ingestion of 50 g CHO in various foods measured as change from basal values in 8 type II diabetic subjects. Mean basal values ranged from 180 ± 21 mg/dl (lentils) to 199 ± 20 mg/dl (oatmeal).

test meal as the glucose response to 50 g glucose is to the insulin response to 50 g glucose, i.e., $G_t/I_t = G_g/I_g$, where G_t is the area under the glucose curve after a test meal, I_t is the area under the insulin curve after a test meal, G_g is the area under the glucose curve after a glucose meal, and I_g is the area under the insulin curve after a glucose meal.

This representation allows for the comparison of insulin and glucose responses without using I/G ratios. By comparing predicted response with the observed (measured) responses, we can use Student's paired *t* test. Whenever a measured negative value is present, a negative predicted value also will be calculated. Student's paired *t* test accommodates these negative values without penalizing the statistical significance. Student's *t* test for paired variates and two-way analysis of variance with least significant difference, as appropriate, were used for analysis of statistical significance. Each patient served as his own control. Data are given as means ± SE. The significance criterion was $P < .05$.

RESULTS

Study 1

Plasma glucose response. Mean fasting plasma glucose was 186 ± 8 mg/dl (range 119–267 mg/dl). After ingestion of 50 g glucose (Fig. 1), plasma glucose reached a peak at 1 h and returned to baseline at 5 h. After the ingestion of potato, oatmeal, or bread, the plasma glucose increase was similar. In each case the peak occurred at 1 h, and 5 h were required for the plasma glucose concentration to return to the fasting value.

After the rice meal, the increase in mean plasma glucose at 1 h was significantly less ($P < .05$) than for the potato, oatmeal, bread, and glucose meals. Subsequently, the decline was comparatively slow. When the curve was extrapolated, 6.5 h were required for it to reach the baseline.

After the ingestion of lentils and kidney beans, plasma glucose increased only slightly, as expected. These peak glucose concentrations were significantly less than for all the other meals ($P < .01$). The rise in plasma glucose concentration also was slower. The maximal glucose concentration occurred at 2 h rather than 1 h. In addition, after the ingestion of lentils, glucose concentration was still slightly elevated after 5 h.

Serum insulin response. Mean fasting serum insulin concentration was 18 ± 1 μU/ml (range 6–36 μU/ml). After ingestion of the glucose meal it reached a peak at 1 h and was still above the fasting level at 5 h (Fig. 2). The peak

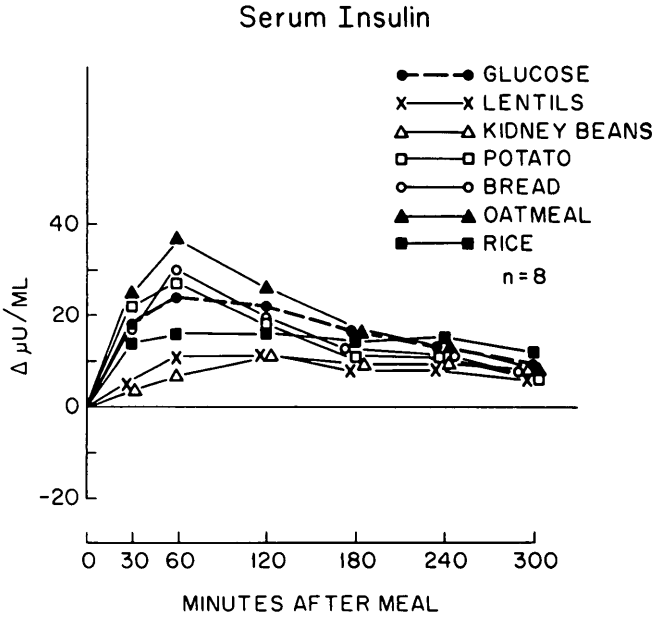

FIG. 2. Serum insulin responses to ingestion of 50 g CHO measured as change from basal values in 8 type II diabetic subjects. Mean basal values ranged from 17 ± 2 μU/ml (potatoes) to 21 ± 2 μU/ml (kidney beans). Peak value after ingestion of lentils and kidney beans was significantly less than for all other meals except rice ($P < .05$).

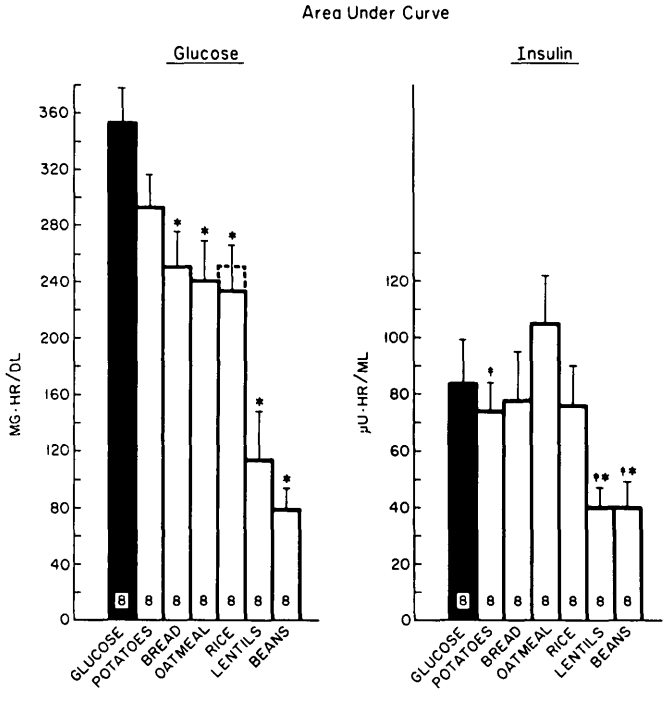

FIG. 3. Mean areas under plasma glucose and serum insulin curves determined over 5 h after ingestion of 50 g CHO in 8 type II diabetic subjects. Mean area under the glucose curve after ingestion of glucose was significantly greater than that for bread, oatmeal, rice, lentils, and kidney beans. Glucose value had not returned to baseline 5 h after ingestion of rice. Consequently, *broken line* indicates net glucose area under curve when extrapolated to baseline (6.5 h). Mean area under insulin curve after ingestion of glucose was significantly greater than that for lentils and kidney beans.
***$P < .05$, statistically different from glucose; ‡$P < .05$, statistically different from oatmeal.**

increases in plasma insulin after the ingestion of potatoes, oatmeal, and bread were similar. After 5 h, the insulin remained modestly elevated even though the glucose concentration had returned to the fasting level. This is probably due to continued stimulation of insulin secretagogues from the gut by modest amounts of food remaining in the upper intestine. A delayed return of the insulin concentration to a fasting value also has been observed previously after ingestion of a CHO meal or a mixed meal in normal (3,4,14) and type II diabetic (6,16; F.Q.N. and M.C.G., unpublished observations) subjects.

After the rice meal, serum insulin increased only slightly at 1 h. However, it then remained elevated and essentially unchanged over the next 4 h. After the ingestion of lentils and kidney beans, the plasma insulin concentration also increased only modestly and was still elevated 5 h after the meal.

Integrated glucose areas. Areas for oatmeal, bread, and rice were similar at 68, 71, and 66% that of the glucose meal. In addition, if the mean curve for rice was extrapolated to the baseline, the area was 71% that of glucose. These areas were all significantly smaller than for glucose (Fig. 3). The area after the potato meal was 83% that of the glucose meal. The net glucose areas after the ingestion of kidney beans and lentils were only 22 and 32% that of the glucose meal, respectively.

Integrated insulin area. Net insulin areas for bread, rice, and potatoes were similar and less than that observed after the glucose meal (93, 90, and 88%, respectively). However, the insulin area after the ingestion of oatmeal was 125% that of the glucose meal. None of these differences in area was statistically significant when compared with the glucose meal results. After the ingestion of lentils and kidney beans, the areas were both 48% that of the glucose meal.

Predicted versus observed insulin area. Observed insulin area was significantly greater than the predicted insulin area for oatmeal, lentils, and beans (Fig. 4) ($P < .05$).

Study 2

Plasma glucose response to cornstarches. Mean fasting glucose concentration (180 ± 10 mg/dl) was similar in these subjects compared with the subjects used in the previous study.

After the ingestion of cornflakes and the low-amylose muffins, the plasma glucose response was similar to that after the glucose meal (Fig. 5). After the ingestion of the high-amylose muffins, the plasma glucose rise was modest. The maximal rise was statistically significantly less compared with that of the other meals ($P < .01$).

Serum insulin response. Mean fasting insulin concentration was 16 ± 1 μU/ml. After the ingestion of 50 g glucose, cornflakes, and high-amylose corn muffins, the peak serum insulin concentrations were similar (Fig. 6). After the ingestion of the low-amylose muffins, the peak insulin value was nearly double that of the other meals.

Glucose and insulin areas over baseline. Net glucose areas for the cornflakes and the low-amylose muffins were 101 and 118% of that for the glucose meal (Fig. 7). They were not significantly different from the glucose meal. Net glucose area for the high-amylose muffins was <52% of that for the other three meals ($P < .05$).

Net insulin areas for the cornflakes, low-amylose muffins, and high-amylose muffins were 133, 161, and 102% of the insulin area for the glucose meal, respectively. These differences were not statistically significant.

Predicted versus observed insulin area. Observed insulin values were higher than the predicted in every case (Fig. 4). However, the difference was only statistically significant after ingestion of high-amylose corn muffins.

Urine glucose excretion over 5 h. The amount of glucose excreted during the 5 h after the ingestion of each meal was as expected considering the rise in plasma glucose concentration after each meal (Table 2). Mean glucose excreted did not exceed 8 g for any of the meals.

Comparison of 3-h areas with 5-h areas. Because many studies in the literature were conducted for 2–3 h, we have included 3-h data from this study and compared the response with the 5-h data. As expected, the 5-h/3-h glucose area

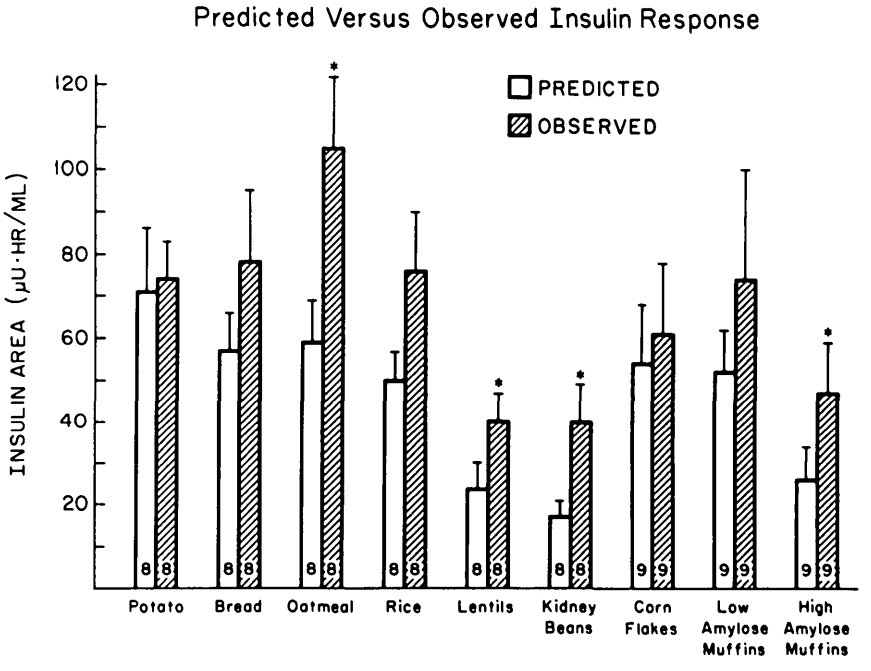

FIG. 4. Predicted versus observed insulin response. *Striped bars* indicate means ± SE for observed (measured) insulin area for each meal. *Open bars* indicate means ± SE for predicted insulin area for each meal. Predicted values were calculated as described in MATERIALS AND METHODS. N = 8 for potatoes, bread, oatmeal, rice, lentils, and kidney beans; N = 9 for cornflakes and low- and high-amylose corn muffins.
*Statistical significance based on Student's paired *t* test.

ratios generally were greatest for those of foods that appeared to have a delayed digestion and absorption. Also the 5-h/3-h insulin area ratios were nearly all greater than the ratio of glucose areas, confirming the delayed return of the insulin concentration to a fasting value (Table 3).

DISCUSSION

Starch is present in plants in the form of structurally defined granules that are unique for each plant (16). Starch granules in cereal grains are structurally different from those in tubers (potatoes), which in turn are different from those in leguminous seeds (beans and peas). There also are differences in the starch granules from different species within each group.

Starch granules are composed of the highly branched polymer amylopectin and the linear polymer amylose. The ratio of the polymers in the granule from different plant sources is genetically defined. This ratio, as well as the amylopectin branching pattern, affects the physical characteristics of the starch both in regard to its response to cooking and its digestibility in the small intestine (16).

Before the starch can be hydrolyzed effectively in the intestine, the granule must be disrupted. This is usually accomplished by heating in water (gelatinization), but grinding with or without a pressure-extrusion technique may also be used (17). In general, high-amylose starch granules are less easily disrupted and are more slowly hydrolyzed by enzymes present in the gut.

In gelatinization, the starch granules are heated in water until the starch granules swell and the crystalline structure is disrupted irreversibly. With increasing amylose content, less swelling occurs because of stronger binding forces within the granules. Indeed, with a very high amylose content, no swelling may be detectable (16), and there is little disruption of the granule.

Effects of the crystalline structure, in addition to amylose content, also have a role in gelatinization. These are probably because of variations in the branching chains in the amy-

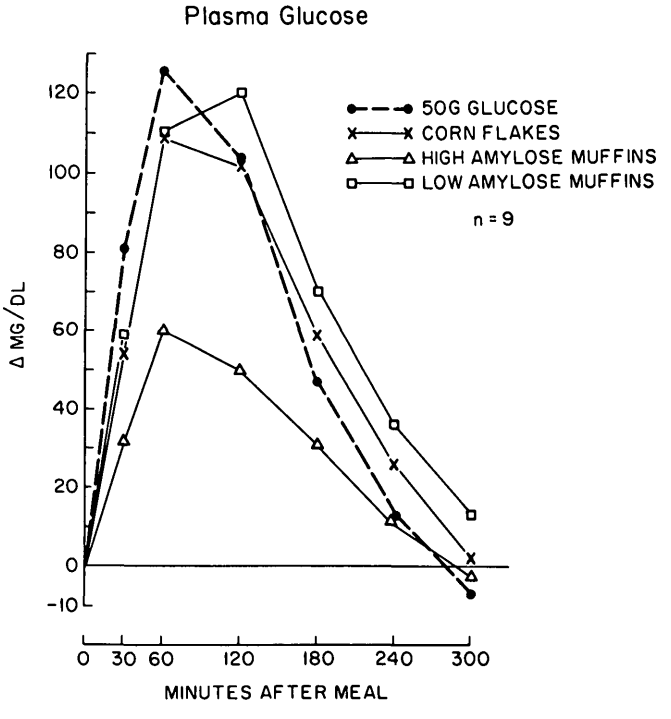

FIG. 5. Plasma glucose response to the ingestion of 50 g CHO measured as change from basal values in 9 type II diabetic subjects. Mean basal values ranged from 170 ± 19 mg/dl (low-amylose corn muffins) to 189 ± 21 mg/dl (glucose).

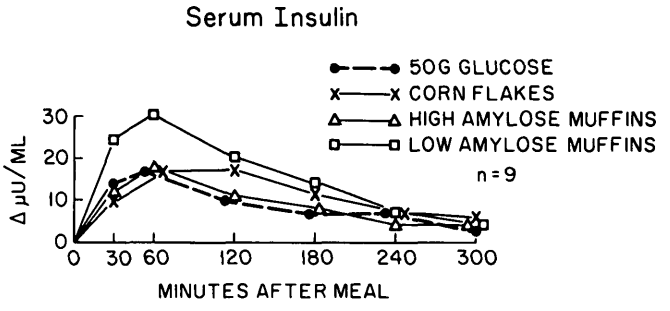

FIG. 6. Serum insulin response to ingestion of 50 g CHO measured as change from basal values in 9 type II diabetic subjects. Basal values ranged from 15 ± 1 μU/ml (glucose) to 17 ± 2 μU/ml (cornflakes).

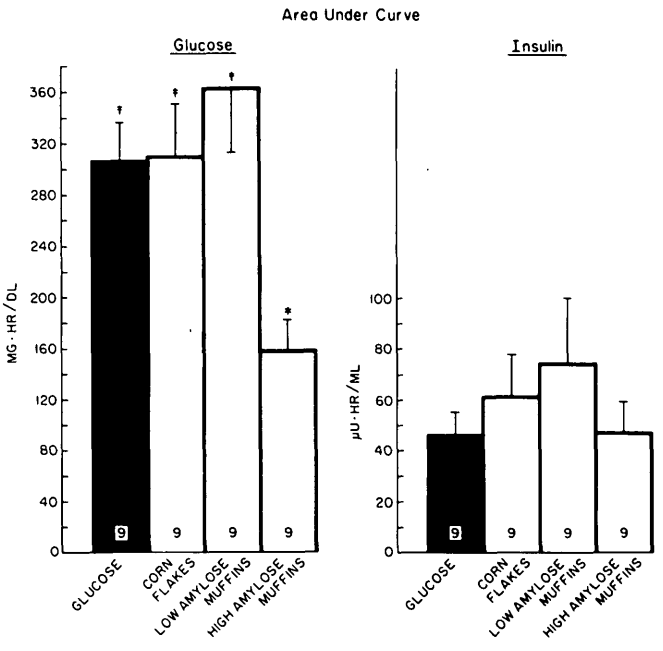

FIG. 7. Mean areas under plasma glucose and serum insulin curves determined over 5 h after ingestion of 50 g CHO as glucose and cornstarch products in 9 type II diabetic subjects.
***Statistically different from glucose; †statistically different from high-amylose muffins.**

lopectin structure, and protein, lipids and other minor nonstarch components present in the granules. For example, rice and potatoes have similar amylose content (17–20%), yet gelatinization for rice occurs at higher temperatures (68–78°C) than for potatoes (55–65°C), and there is less disruption with short-time boiling. With less disruption of the granules, there is less exposure to the hydrolyzing enzymes of the gut, which may delay overall digestion and absorption but not necessarily total net absorption (16).

In our study the plasma glucose rise after rice ingestion was lower than for the other cereal starches and for potatoes; however, the glucose concentration remained elevated longer. This is compatible with slower digestion for rice starch.

The plasma glucose and serum insulin patterns for the potato, rice, bread, and glucose meals over the first 3 h of our study were similar to those of untreated type II diabetic subjects studied by Crapo et al. (18). However, in both studies, at 3 h the plasma glucose and serum insulin concentrations were still considerably above the fasting values. By extending our study period to 5 h, the time required for the plasma glucose to return to a basal level after glucose administration, the apparent reduction in net glucose area after the ingestion of rice compared with other starches reported by these investigators was considerably less and was not statistically significantly different (18). In fact, after the initial rise the plasma glucose values decreased very slowly after ingestion of the rice, and at the end of 5 h it was higher than for any of the other starches tested. In addition, the serum insulin area over the last 2 h after the meal was greatest after the rice meal. The overall result was an insulin area for

TABLE 3
Comparison of 5- and 3-h glucose and insulin areas

	Glucose area			Insulin area		
	5 h	3 h	5-h/3-h ratio	5 h	3 h	5-h/3-h ratio
Study 1						
Glucose	353	267	1.33	84	62	1.36
Potato	293	220	1.33	74	55	1.36
Bread	251	196	1.28	78	56	1.39
Oatmeal	241	201	1.20	105	75	1.40
Rice	234	163	1.44	76	45	1.69
Lentils	114	76	1.50	40	26	1.54
Beans	79	61	1.30	40	22	1.82
Study 2						
Glucose	306	283	1.08	46	37	1.24
Cornflakes	309	260	1.19	61	45	1.36
Low amylose	362	291	1.24	74	66	1.12
High amylose	158	138	1.14	47	38	1.24

the rice meal that was similar to that for the bread and potato meals (Fig. 3). This also was different from the response noted by Crapo et al. (18). Others also have used the 2- or 3-h postmeal response in comparing glucose areas (7–10,19). From our data, it is apparent that this amount of time is inadequate when diabetic subjects are studied. Three-hour measurements have the tendency to understimulate the true net glucose and insulin responses to food substances, and this is exaggerated when delayed or prolonged digestion and absorption are present. More accurate data are obtained when glucose and insulin responses are determined over a period sufficient for the glucose and insulin concentrations to approach the fasting value.

Jenkins et al. (9) also studied diabetic subjects for only 3 h after a meal. In addition, after the ingestion of bread, oatmeal, rice, and beans, the areas calculated over 3 h for the diabetic subjects studied by these authors were greater than for our subjects over 5 h after comparable CHO meals. This is probably because the subjects studied by them had more severe diabetes. Also, 10 of the 12 subjects studied required insulin, and the other 2 were on oral agents. Thus, it is difficult to directly compare their results with those of our study.

The observation that oatmeal ingestion resulted in the greatest mean insulin area in terms of the absolute area when compared with other high-starch foods is intriguing (Fig. 3). The difference was statistically significant when compared with potatoes but not with bread or rice. However, it was significant when these three foods were considered as a group ($P < .05$). In addition, the observed insulin response was significantly greater than the predicted based on the glucose rise (Fig. 4). The reason for the increased insulin response is not known. However, it may at least partly explain the success of the oatmeal and milk diet advocated by Von-Noorden (20) at the turn of the century.

We were particularly interested in the glucose and insulin response to the ingestion of lentils and kidney beans. It has been shown consistently that the ingestion of starch in the form of legumes results in a much smaller postmeal glucose area than that observed after the ingestion of comparable amounts of starch in cereal grains and potatoes. This has been demonstrated in normal (21) and diabetic (9) subjects. The smaller glucose area can be explained by the relatively slow or incomplete hydrolysis of the starch in legumes by intestinal enzymes (22,23). The reason for this is not well understood and is probably complex. Phenolic compounds such as tannins and catechins are common in legumes and bind both protein and carbohydrate. This binding interferes with digestion but may be reversed by heating (24). Also the starch in legumes has a relatively high amylose content (16). The latter cannot entirely explain the small glucose rise, because the ingestion of a high-amylose cornstarch resulted in a greater glucose rise than that observed with the legume meals (Fig. 5).

In addition to starch, legumes contain a large amount of protein. Generally the ratio is ~2:1, respectively (Table 1). We previously reported that protein in the form of ground beef was just as potent as glucose in stimulating insulin secretion in type II diabetic subjects and resulted in a modest decrease in glucose concentration. The simultaneous ingestion of beef with glucose resulted in a synergistic effect on the serum insulin response (5). Therefore, the considerably greater than predicted insulin response was as might be expected from the protein content of the legumes. Whether this is indeed due to protein remains to be determined.

In our subjects, cornstarch muffins containing 0–7% amylose produced a net glucose area that was 119% of that produced by glucose ingestion. This difference approached statistical significance ($P < .10$). Cornflakes containing 25–30% amylose produced a net glucose area not significantly different from glucose. The high-amylose (65–75%) cornstarch muffins produced a glucose area that was ~50% of that for the other cornmeals. These data confirm the importance of the amylose content on the digestibility of starch (25). Actually, a 10% greater plasma glucose area might be anticipated for all starch-containing foods compared with a comparable mass of glucose, because starch consists of anhydrous glucose units. When values less than this are observed, incomplete digestion of the starch may be suspected. In agreement with Jenkins et al. (9), ingestion of cornflakes resulted in the greatest postmeal glucose area of any commercially available food tested.

The cornstarch muffins contained a relatively large amount of fat. However, this did not delay the rise in glucose concentration, nor did it appear to reduce the total glucose area response. A similar lack of effect of fat ingestion on glucose rise has been observed previously after ingestion of a mixed meal as the first meal of the day. It did effect the glucose rise after meals ingested later in the day (4).

In summary, these data suggest that high-amylose starch foods may be useful in the diet for type II diabetic people provided they are acceptable to the patient. The muffins used in this study were considered palatable by our patients as a single meal, although they were not enthusiastic about them. Whether better food formulations with this starch will result in a more acceptable product remains to be determined.

ACKNOWLEDGMENTS: We thank the patients for participation in this study and the staff of the STDU and the laboratory for assistance.

This study was supported by a grant from the Veterans Administration.

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