Temporal study of metabolic change when poorly controlled noninsulin-dependent diabetics change from low to high carbohydrate and fiber diet[1-3]

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ABSTRACT Thirteen poorly controlled noninsulin-dependent diabetic subjects ingested in succession over 5.5 wk their usual low-carbohydrate, low-fiber diet (LCF) for 3 d, a high-carbohydrate, high-fiber diet (HCF) for 3 wk, and the LCF diet again for 2 wk. All diets were designed to be individually isoenergetic. Fasting plasma glucose fell significantly during the HCF diet and then rose significantly during the last LCF diet. Dietary change rather than hospitalization had its full effect by 18 d. Urinary glucose excretion rose transiently on the HCF diet before also falling significantly. Similarly, pancreatic immunoreactive glucagon (IRG) fell significantly on the HCF diet and increased significantly on the LCF diet. No significant differences were observed in plasma insulin, serum free fatty acids, or monocyte insulin binding activity between the two diets. Reduction in circulating IRG may in part explain the lower fasting (or basal) plasma glucose observed on HCF diets. *Am J Clin Nutr* 1988; 48:104–9.

KEY WORDS High carbohydrate, high fiber, diets, diabetes, insulin, FFA, glucagon, insulin receptor

Introduction

Controlled (1–3) and uncontrolled (4) studies indicated that diets high in carbohydrate and dietary fiber (HCF) from natural sources improve control of diabetes predominantly by lowering the basal (fasting) plasma glucose level. The time course of this change has been poorly documented in uncontrolled studies (4) and thus the concept that the improvement is induced over a period of days is poorly appreciated. The mechanism of the improved control is uncertain although evidence does suggest that there is an enhancement of insulin sensitivity (1, 2, 5). In both insulin-dependent diabetes mellitus (IDDM) (6) and noninsulin-dependent diabetes mellitus (NIDDM) (7, 8) an increase in monocyte receptors was observed when plasma glucose was lowered on these diets. Free fatty acids (FFA) and pancreatic glucagon, the other factors that potentially affect apparent insulin sensitivity, have not been studied in NIDDM patients after transfer to an HCF diet.

We sought to distinguish between the effects of hospitalization and dietary change on the temporal changes in carbohydrate (CHO) metabolism after altering the amount of absorbable CHO and fiber in the diet of NIDDM patients. We started with a baseline period of the patient's usual low-CHO, low-fiber (LCF) diet and demonstrated a reversal of the induced metabolic change on the HCF diet when patients were returned to the LCF diet during continued hospitalization. In addition, we investigated the effect of such a dietary change on serum FFA, pancreatic glucagon levels, and monocyte insulin receptors.

Subjects and methods

Subjects

Thirteen poorly controlled NIDDM patients were recruited from the Diabetic Clinic, an outpatient facility. Poorly controlled patients were those who had postbreakfast (~2 h) plasma glucose levels > 11 mmol/L for at least the preceding 6 mo. All required additional treatment to lower plasma glucose and agreed to participate in this dietary study during which de-

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tailed dietary education could be provided. The study was approved by Prince Henry's Hospital's Research (Advisory and Ethics) Committee. Twelve patients were admitted to the hospital for the duration of the study and one remained an outpatient. Characteristics of the patients are shown in **Table 1.** Three patients received diet therapy and ten received sulphonylurea treatment plus diet therapy.

Diets

An experienced dietitian interviewed all patients to obtain details of their actual LCF diets. (Twenty-four hour recall, checklist of major food items, and dietary record from hospital history were used.) Individually isoenergetic HCF diets high in unrefined CHO were designed. The diets of one subject are illustrated in **Table 2.** The average nutrient content for all subjects is shown in **Table 3.** The macronutrient content was calculated from published tables (10–12) (analysis performed with the food analysis program (13) at Deakin University, Geelong, Victoria). Legumes apart from garden peas and string beans were not used. The low level of the contribution of CHO to energy intake (28 ± 1.5%) in the total diet of the patients is not a reflection of current nutrition policy for Australians with diabetes.

Protocol

After a 3-d baseline period (referred to as week 1) on their usual LCF diet, the subjects were transferred to an HCF diet for 3 wk. The subjects then returned to their normal LCF diet for a further 2 wk. Diet changes all occurred on Thursdays and patient admissions were planned so that a 3-d baseline could be achieved before the first Thursday. Time periods were based on previous experience cited by Simpson et al as unpublished observations (1, 2) which showed that ~2 wk is required for baseline plasma glucose to change significantly after a dietary change. For the 12 inpatients meals were individually prepared by the dietitian in the diet kitchen and delivered individually to the subjects. Consumption of meals was supervised and patients were encouraged to eat all the food served to them. Detailed dietary instruction was given to the outpatient subject (and spouse) for the midday and evening meals; breakfast was individually prepared in the diet kitchen and daily in the hospital.

Daily fasting blood samples (including 2 mL added to 3 mg aprotinin [Trasylol®, Bayer AG, Leverkusen, FRG]) were taken and placed on ice before the plasma or serum were separated and stored at −20 °C. Continuous 24-h urine collections were performed. Patients were weighed daily.

During weeks 1, 4, and 6, 80 mL blood was taken into heparinized syringes from seven patients for monocyte insulin-receptor studies.

Analytical methods

Plasma and urine glucose were assayed on a Yellow Springs glucose analyzer (Yellow Springs Instrument Co, Yellow Springs, OH). Plasma insulin was estimated by radioimmunoassay (14). Pancreatic immunoreactive glucagon (IRG) was assayed by radioimmunoassay (15) with S Bloom antiserum RCS-5 (M Sissons, St Vincent's Hospital, Melbourne). Serum lipids were estimated in fasting serum by established clinical assays: serum triglycerides by the glycerol kinase method (Boehringer Kit, catalogue #240-052, Boehringer Mannheim, Mannheim, FRG); HDL cholesterol by polyethylene glycol 6000 precipitation of low-density lipoprotein (LDL); and very LDL and cholesterol (HDL and total) by a colorimetric method (Boehringer Enzymatic CHOD-PAP Kit, catalogue #236691, Boehringer Mannheim). FFA were estimated by Dr CS Lo (Deakin University, Geelong) with a double-extraction colorimetric method (16). Mononuclear cell suspensions from seven patients on three occasions and seven normal subjects (laboratory personnel, aged 31.3 ± 2.8 y, percentage of ideal body weight of 119.3 ± 6.8%) were prepared from heparinized blood according to the method of Boyum (17), washed in phosphate-buffered saline (pH 7.8), and suspended in assay buffer containing 1% bovine serum albumin (Miles Laboratory, Miles Scientific, Naperville, IL). Monoiodinated (I^{125}) insulin was obtained initially from the Royal Children's Hospital, Melbourne (Dr M Dunlop; specific activity, 150 μCi/μg [5.55 MBq/μg]; used for three patients) and subsequently from Novo Research Laboratories (A14-labeled; specific activity, 200 μCi/μg [7.40 MBq/μg]; used for four patients). Insulin-I^{125} ($10–13 \times 10^{-3}$

TABLE 1
Characteristics of subjects

Subject no	Sex	Age	Percent IBW*	Duration	Treatment†	Fasting plasma glucose
		y		*y*		*mmol/L*
1	M	54	149	7	Su	11.9
2	F	70	108	6	Su	11.7
3	M	52	113	11	D	7.9
4	M	60	85	7	Su	11.3
5	M	68	98	5	D	12.0
6	F	50	168	2	Su	7.6
7	M	58	110	6	Su	10.9
8	M	57	98	17	Su	14.2
9	M	74	130	7	Su	11.1
10	M	72	153	5	Su	10.0
11	F	74	189	3	Su	20.5
12	M	64	141	6	D	11.1
13	M	66	158	3	Su	11.8
Mean ± SEM		63 ± 2	131 ± 9	6.5 ± 1.1		11.7 ± 0.9

* Percent IBW = percentage of ideal body weight (9).
† D = diet only; Su = sulphonylurea plus diet.

TABLE 2
One subject's daily menu for the low-carbohydrate, low-fiber and high-carbohydrate, high-fiber

LCF diet		HCF diet	
Breakfast			
100 g	pineapple	100 g	unsweetened peaches
17 g	All Bran®	17 g	bran cereal
32 g	whole-wheat bread	96 g	whole-wheat bread
14 g	margarine	10 g	margarine
45 g	poached egg	110 g	grilled tomatoes
		230 mL	skimmed milk
Snack			
16 g	sweet plain biscuits	100 mL	orange juice
		150 g	pear
Lunch			
130 g	grilled steak	130 g	lean rump steak
70 g	mashed potato	160 g	rice
70 g	corn	35 g	cabbage, boiled
60 g	green beans	60 g	pumpkin, boiled
	baked custard (230 mL milk, 50 g egg)	280 g	baked potatoes
		100 g	unsweetened pineapple
		96 g	whole-wheat bread
100 g	pear	5 g	margarine
Snack			
12 g	dry biscuit	100 g	apple
20 g	cheese		
7 g	margarine		
Dinner			
150 g	minced steak	110 g	chicken
40 g	rice	90 g	potato
32 g	whole-wheat bread	20 g	lettuce
7 g	margarine	30 g	cucumber
20 g	lettuce	30 g	celery
55 g	tomato	60 g	beetroot
15 g	celery	6 g	prunes
50 g	broccoli	110 g	grilled tomatoes
		100 g	unsweetened pears
		96 g	whole-wheat bread
		5 g	margarine
Snack			
130 g	orange	100 g	banana
230 mL	milk		
2.310 kcal		2.335 kcal	
30% carbohydrate		57% carbohydrate	
52% fat		25% fat	
18% protein		18% protein	
27 g fiber		66 g fiber	

pmol) and varying concentrations of native insulin (0–320 pmol/L) were incubated with the mononuclear cells (mean number of cells per culture, 5.2×10^6) at 15 °C. All incubations were carried out in duplicate. After a 2-h incubation cell-bound radioactivity was separated by microfuge centrifugation at 4 °C of 100-μL duplicates through dibutylphthalate (BDH). Nonspecific binding (NSB) was defined as the remaining bound radioactivity in the presence of 1 μmol/L native insulin. Specific binding was calculated by subtracting NSB from total binding and the count was expressed per 5×10^6 monocytes per milliliter (proportion of monocytes determined by nonspecific esterase staining [18]). At the tracer-only point the intraassay and interassay CVs were 6.1 and 16.5%, respectively.

Data analysis

Results are expressed as mean ± SEM. Comparison between fasting levels of plasma glucose, insulin, IRG, FFA, cholesterol, HDL cholesterol, serum triglycerides (log-transformed), and daily weights were made by a two-way analysis of variance (two-way ANOVA) (19) with time and patient as the factors. The reference time was day 3 of the baseline LCF dietary period. Comparisons between time points for the 24-h urine glucose levels were made by the Wilcoxon matched-pairs test (19) because data were nonparametric. ANOVA (19) was used to compare the percentages for the baseline values for specific insulin binding to the monocytes with those at the end of the two dietary periods.

Results

Weight

Although the different diets were designed to be isoenergetic most patients gradually lost a small amount of weight (**Fig 1**). The mean loss of 1 kg during the HCF diet was significant ($p < 0.01$), whereas the further mean change of 0.5 kg during the LCF diet was not significant ($p > 0.05$).

Fasting plasma glucose

During the first 3 d of the study while the subjects received their usual diet (LCF), no significant change occurred in fasting plasma glucose (Fig 1). The plasma glucose then fell significantly from 11.0 ± 1.1 mmol/L (day 3) to 8.2 ± 1.0 mmol/L ($p < 0.01$) after 18 d on the HCF diet (day 21 of study). Two-way ANOVA allows comparisons to be made between all time points and we chose to compare day 3 of the first LCF diet with day 18 of the HCF diet because day 3 was the last day of the baseline period and day 18 (HCF) was the nadir for fasting plasma glucose. Thereafter no further significant change occurred during the HCF diet, which lasted 22 d. After changing to the LCF diet (day 25 of the study) plasma glucose changed little for several days before rising gradually (day 27 of the study) from 8.5 ± 1.0 mmol/L to 10.0 ± 1.0 mmol/L ($p < 0.01$) at the end of the study (day 38). Twelve of the 13 patients showed the same directional change in fasting plasma glucose during the study.

Urinary glucose excretion

Values for urinary glucose fluctuated greatly for individual patients throughout the dietary periods (Fig 1).

TABLE 3
Daily energy and macronutrient content of the low-carbohydrate, low-fiber and high-carbohydrate, high-fiber diets*

	LCF	HCF
Energy (kcal)	1.992 ± 0.088	1.992 ± 0.088
Protein (%)	22.0 ± 1.1	19.1 ± 0.9
Fat (%)	49.2 ± 2.1	21.3 ± 1.0
Carbohydrate (%)	28.0 ± 1.5	60.0 ± 2.3
Sugars (%)	11.5 ± 0.9	24.1 ± 1.1
Starch (%)	16.5 ± 0.5	36.2 ± 2.1
Fiber (g)	21.4 ± 1.3	56.8 ± 2.2

* Mean ± SEM. Macronutrient content is expressed as percentage of total energy. Sugars represent all the free monosaccharides and disaccharides including lactose.

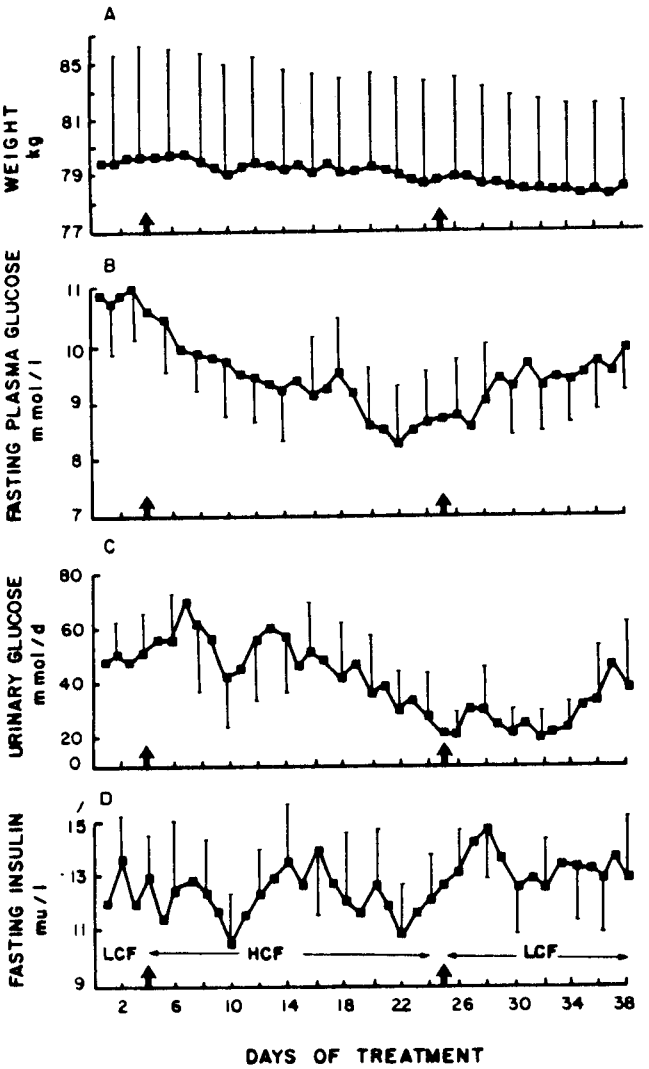

FIG 1. Daily weight (A), fasting plasma glucose (B) and insulin (D), and urinary glucose loss (C) during the 38 d of the study. The vertical arrows indicate first full day of new diet. HCF = high-carbohydrate, high-fiber diet; LCF = low-carbohydrate, low-fiber diet. ($\bar{x} \pm$ SEM; alternate SEM not plotted for sake of clarity.) (To convert mU/L to pmol/L, multiply by 7.175.)

There was a significant rise ($p < 0.01$, Wilcoxon matched-pairs test) from the baseline level to a peak value of 92 mmol/d (mean) during the first week; the peak occurred on different days for different subjects. Thereafter there was a gradual fall in urinary glucose excretion to a mean of 27.3 mmol/d on day 24; the difference between baseline levels and values at the end of the HCF period was highly significant ($p < 0.01$). No further significant change in glucose excretion occurred during the LCF period although there was a trend toward increasing urinary glucose loss by end of the study.

Fasting insulin

The fasting insulin levels fluctuated throughout both dietary periods and no constant pattern emerged (Fig 1). The levels were not significantly different at the beginning or end of either dietary period.

Insulin receptors

Unfortunately, receptor studies were performed on only seven patients because insulin tracer was not available during some inpatient studies. The specific insulin binding to circulating monocytes at different stages of the study is shown in **Figure 2.** There was no difference in the insulin-binding profile of the patients at any stage of the study. The mean displacement curve for each of weeks 1, 4, and 6 is shown together with the range observed for the seven normal subjects.

Fasting free fatty acids

FFA levels at the end of each week are shown in **Table 4.** Two fasting samples taken on successive days were averaged for each patient. There was no significant change (two-way ANOVA) in FFA levels either during or between different dietary periods.

Serum triglycerides

Serum triglycerides fell significantly during the HCF dietary period ($p < 0.001$ between weeks 1 and 4) (Table 4). The change in levels during the subsequent LCF diet was not statistically significant.

Serum cholesterol

Serum cholesterol also fell significantly during the HCF diet (week 1 vs week 4, $p < 0.001$) but then rose significantly during the LCF diet (week 4 vs week 6, $p < 0.001$) (Table 4).

HDL cholesterol

The HDL cholesterol followed the same pattern as total cholesterol although the differences were just barely significant ($p < 0.05$ for week 1 vs week 4 and for week 4 vs week 6) (Table 4). The HDL-cholesterol-to-total-

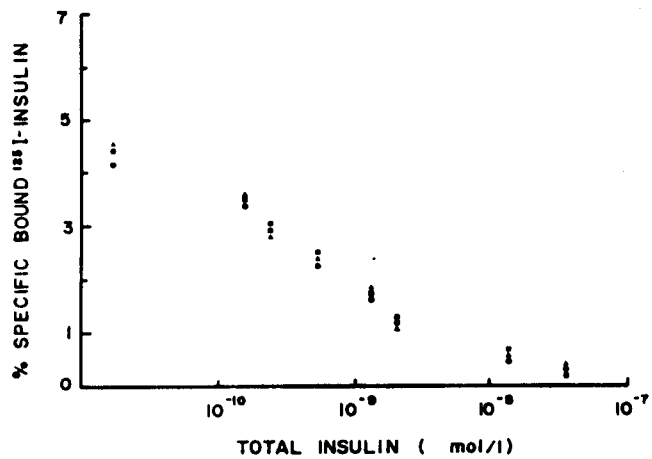

FIG 2. Mean percentage specific insulin-I^{125} binding to circulating monocytes (expressed as 5×10^6 monocytes/mL) on week 1 (LCF diet ●), week 4 (HCF diet ■), and week 6 (LCF diet ▲). Shaded area = range of specific insulin binding observed in seven normal subjects.

TABLE 4
Fasting FFA levels and serum lipids at the end of each week*

	Baseline LCF	HCF			LCF	
Week	1†	2	3	4	5	6
Fasting FFA‡ (μmol/L)	552 ± 67	591 ± 59	578 ± 68	564 ± 51	548 ± 73	558 ± 76
Triglycerides (mmol/L)	2.92 ± 0.36	2.32 ± 0.22	2.07 ± 0.24	2.20 ± 0.28	2.06 ± 0.29	2.00 ± 0.26
Total cholesterol (mmol/L)	6.14 ± 0.26	5.73 ± 0.27	5.19 ± 0.29	5.20 ± 0.24	5.49 ± 0.38	5.78 ± 0.36
HDL cholesterol (mmol/L)	1.11 ± 0.16	1.05 ± 0.10	1.04 ± 0.14	0.99 ± 0.10	1.04 ± 0.10	1.11 ± 0.12

* Mean ± SEM.
† Week 1 represents only 3 d.
‡ FFA levels are the mean of samples taken on two consecutive days.

cholesterol ratios were remarkably constant throughout each period (0.18, 0.19, and 0.19 for weeks 1, 4, and 6, respectively).

Fasting immunoreactive glucagon

Samples from three patients were lost through a freezer failure. IRG was measured in 10 samples for the other 10 patients for the days shown in **Table 5**. IRG levels were significantly lower on days 21–25 at the end of the HCF diet than during the baseline LCF period ($p < 0.05$ or < 0.01 for all comparisons between the two baseline LCF samples and each of the values between days 21 and 25; two-way ANOVA). Immediately after patients returned to the LCF diet (days 27 and 29) IRG rose significantly compared with days 21–25 ($p < 0.05$, or < 0.01). The levels at the end of LCF diet (days 36 and 38) were not significantly different from either those on days 27 and 29 or those on days 2 and 4 (baseline LCF).

Discussion

Many studies (1, 2, 4) showed that diets high in CHO and fiber using nonleguminous foods, as in this study, will lower the plasma glucose in diabetic patients. Ours and earlier studies (1, 2, 3) emphasized the importance of HCF diets in lowering basal (fasting) plasma glucose. Our study also confirms the earlier uncontrolled observation (4) that the lowering of basal plasma glucose occurs gradually over several days after a change of HCF diet. Basal plasma glucose then rises gradually when the diet is altered to a more traditional LCF diet, which indicates that the effect on plasma glucose levels is not merely a hospitalization effect. The fall in fasting plasma glucose leveled off after 18 d on the HCF diet. We cannot rule out the possibility of an effect of the HCF diet caused by the slightly reduced energy content, contributing to the 1-kg weight loss on that diet. Weight loss is often seen with such diets despite the intention that the HCF diet be isoenergetic with the LCF diet. However, on the subsequent LCF diet 0.5 kg more was lost while fasting plasma glucose rose.

This study also highlights the increase in urinary glucose excretion that occurs at the beginning of the HCF diet. The increased glycosuria was not clinically significant and persisted for only a few days before it also decreased on the HCF diet.

The mechanism of lowering the basal plasma glucose by HCF diets is unclear although it appears to involve an enhancement of insulin sensitivity (1, 2, 5). Although previous research found increased insulin receptor binding on HCF diets in NIDDM (7, 8) and IDDM (6) our study did not demonstrate any change between the two diets. In one study of NIDDM (7) the changes were observed 6 wk after the dietary change. A recent report (8) indicated that insulin binding to adipocytes and monocytes in NIDDM increased after 3 wk on an HCF diet. The reasons for the apparent discrepancy between these studies and the current study are unclear. The interassay CV for the tracer-only (insulin-I^{125}) binding point of our assay was 16.5%. If the diet-induced changes had been less than this we could not have detected a change in receptor binding, which might have anticipated the plasma glucose change.

FFA are known to decrease glucose uptake into the

TABLE 5
Fasting immunoreactive glucagon (IRG) levels*

	Baseline LCF		HCF				LCF			
Day†	2	3	19	21	23	25	27	29	36	38
Fasting IRG levels										
ng/L	57.3 ± 13.2	61.6 ± 12.8	40.8 ± 10.4	35.8 ± 27.3	37.9 ± 10.6	33.9 ± 19.4	56.3 ± 11.3	53.4 ± 11.4	49.1 ± 9.5	53.9 ± 10.2
pmol/L	16.4 ± 3.8	17.7 ± 3.7	11.7 ± 3.0	10.3 ± 7.8	10.9 ± 3.0	9.7 ± 5.6	16.2 ± 3.2	15.3 ± 3.3	14.1 ± 9.5	15.5 ± 2.9

* Mean ± SEM; $n = 10$.
† Days 2 and 3 = week 1; days 19–25 = week 4; days 27–29 = week 5; days 36–38 = week 6.

cell (20) and appear therefore to decrease insulin sensitivity. In our study serum FFA concentrations were not affected by the dietary change. Therefore, changes in serum FFA levels do not appear to play a role in modulating insulin sensitivity to the dietary change in this study. Fasting IRG levels were significantly lower on the HCF than the LCF diet. Pancreatic glucagon is involved in the maintenance of fasting plasma glucose levels in man (21, 22) because it modulates hepatic glucose release. In non-diabetics fasting glucagon levels are increased by low CHO intakes (23) whereas in diabetic patients average daily levels are reduced by high dietary fiber intake (24). In our study the lower fasting plasma glucose levels could be causally related to the lower IRG concentrations. The early rise in IRG levels after subjects changed back to the LCF diet, which preceded the rise in plasma glucose, however, suggests that additional factors are involved.

As several other studies showed, HCF diets either lower (25) or have no effect (1, 2) on fasting triglyceride levels. In this study the small weight loss in addition to the HCF dietary change may have contributed to the lowering of serum triglycerides. The serum triglycerides did not show a transient rise in levels early after commencement of the HCF diet. Changes in serum cholesterol on the HCF and later on the LCF diet are consistent with many other reports (1–4, 25). The HDL cholesterol level changed in parallel with the total cholesterol such that the HDL-cholesterol-to-total-cholesterol ratio was unaffected by the dietary changes.

Thus, HCF diets slowly induce a lowering of the basal plasma glucose over a period of 2–3 wk. There is a transient but clinically insignificant increase in glycosuria when the HCF diet is commenced. The mechanism of the lowering of the basal plasma glucose on an HCF diet may involve a lowering of basal IRG levels.

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References

1. Simpson RW, Mann JI, Eaton J, Moore RA, Carter RD, Hockaday TDR. Improved glucose control in maturity onset diabetics treated with high carbohydrate-modified fat diet. Br Med J 1979;1: 1753–6.
2. Simpson RW, Mann JI, Eaton J, Carter RD, Hockaday TDR. High-carbohydrate diets in insulin-dependent diabetics. Br Med J 1979;2:523–5.
3. Simpson HCR, Simpson RW, Lousley S, et al. A high carbohydrate leguminous fiber diet improves all aspects of diabetic control. Lancet 1981;1:1–5.
4. Anderson JW, Ward K. High-carbohydrate, high-fiber diets for insulin-treated men with diabetes. Am J Clin Nutr 1979;32:2312–21.
5. Himsworth HP. The dietetic factor determining the glucose tolerance and sensitivity to insulin of healthy man. Clin Sci 1935;2:67–94.
6. Pedersen O, Hjøllund E, Lindskov HO, Helms P, Sørensen NS, Ditzel J. Increased insulin receptor binding to monocytes from insulin-dependent diabetics after a low fat, high starch, high fiber diet. Diabetes Care 1982;5:284–91.
7. Ward GM, Simpson RW, Simpson HCR, Naylor BA, Mann JI, Turner RC. Insulin receptor binding increased by high carbohydrate low fat diet in non insulin-dependent diabetics. Eur J Clin Invest 1982;12:93–6.
8. Hjøllund E, Pedersen O, Richelsen B, Beck-Nielsen H, Sørensen NS. Increased insulin binding to adipocytes and monocytes and increased insulin sensitivity of glucose transport and metabolism in adipocytes from non insulin-dependent diabetics after a low fat/high starch/high fiber diet. Metabolism 1983;32:1067–75.
9. Metropolitan Life Insurance Company. New weight standards for men and women. Stat Bull Metropol Life Insur Co 1959;40:1–4.
10. Paul AA, Southgate DAT. McCance and Widdowson's the composition of foods. 4th ed. London: Her Majesty's Stationery Office, 1978. (Medical Research Council Special Reports Series #297.)
11. Thomas S, Corden M. Tables of composition of Australian foods (1970). Canberra: Commonwealth Department of Health, Australian Government Public Service, 1970.
12. Southgate DAT, Paul AA, Dean AC, Christie AA. Free sugars in foods. J Hum Nutr 1978;32:335–47.
13. Paul AA, Southgate DAT. McCance and Widdowson's the composition of foods. 4th ed. London: Her Majesty's Stationery Office, 1978.
14. Albano JDM, Ekins RP, Maritz G, Turner RC. A sensitive, precise radioimmunoassay of serum insulin relying on charcoal separation of bound and free hormone moieties. Acta Endocrinol 1972;70: 487–509.
15. Alford FP, Bloom SR, Nabarro JDN. Glucagon levels in normal and diabetic subjects. Use of a specific immunoabsorbent for glucagon immunoassay. Diabetologia 1979;13:1–6.
16. Laurell S, Tibbling G. Colorimetric microdetermintion of free fatty acids in plasma. Clin Chim Acta 1967;16:57–62.
17. Boyum A. A separation of leukocytes from blood and bone marrow. Scand J Clin Lab Invest [Suppl 97] 1968;21:77–89.
18. Yan LT, Li Cy, Crosby WH. Cytochemical identification of monocytes and granulocytes. Am J Clin Pathol 1971;55:283–90.
19. Siegel S. Nonparametric statistics for the behavioural sciences. Tokyo: McGraw-Hill Kogakusha Ltd, 1959.
20. Lassers BW, Kaijser L, Wahlqvist ML, Carlson LA. Relationship in man between plasma free fatty acids and myocardial metabolism of carbohydrate substrates. Lancet 1971;2:448–50.
21. Alford FP, Bloom SR, Nabarro JDN, et al. Glucagon control of fasting glucose in man. Lancet 1974;2:974–9.
22. Gerich JE, Lorenzi M, Schneider V, et al. Effects of somatostatin on plasma glucose and glucagon levels in human diabetes mellitus. N Engl J Med 1974;291:544–7.
23. Muller WA, Faloona GR, Unger RH. The influence of the antecedent diet upon glucagon and insulin secretion. N Engl J Med 1971;285:1450–4.
24. Miranda PM, Horwitz DL. High-fiber diets in the treatment of diabetes mellitus. Ann Intern Med 1978;88:482–6.
25. Anderson JW, Chen WJL, Sieling B. Hypolipidemic effects of high carbohydrate, high fiber diets. Metabolism 1980;29:551–8.