Dietary Fiber, Glycemic Load, and Risk of NIDDM in Men

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OBJECTIVE — Intake of carbohydrates that provide a large glycemic response has been hypothesized to increase the risk of NIDDM, whereas dietary fiber is suspected to reduce incidence. These hypotheses have not been evaluated prospectively.

RESEARCH DESIGN AND METHODS — We examined the relationship between diet and risk of NIDDM in a cohort of 42,759 men without NIDDM or cardiovascular disease, who were 40–75 years of age in 1986. Diet was assessed at baseline by a validated semiquantitative food frequency questionnaire. During 6-years of follow-up, 523 incident cases of NIDDM were documented.

RESULTS — The dietary glycemic index (an indicator of carbohydrate's ability to raise blood glucose levels) was positively associated with risk of NIDDM after adjustment for age, BMI, smoking, physical activity, family history of diabetes, alcohol consumption, cereal fiber, and total energy intake. Comparing the highest and lowest quintiles, the relative risk (RR) of NIDDM was 1.37 (95% CI, 1.02–1.83, P trend = 0.03). Cereal fiber was inversely associated with risk of NIDDM (RR = 0.70; 95% CI, 0.51–0.96, P trend = 0.007; for >8.1 g/day vs. <3.2 g/day). The combination of a high glycemic load and a low cereal fiber intake further increased the risk of NIDDM (RR = 2.17, 95% CI, 1.04–4.54) when compared with a low glycemic load and high cereal fiber intake.

CONCLUSIONS — These findings support the hypothesis that diets with a high glycemic load and a low cereal fiber content increase risk of NIDDM in men. Further, they suggest that grains should be consumed in a minimally refined form to reduce the incidence of NIDDM.

Various aspects of diet that increase insulin resistance or insulin have been hypothesized, over the long term, to influence the risk of NIDDM (1,2). In particular, animal fat may increase and dietary fiber may decrease insulin levels (3). In some clinical studies a beneficial effect of a high-fiber diet on insulin demand in NIDDM subjects has been suggested (4,5). Also, in metabolic studies, carbohydrates with a high glycemic index (a qualitative indicator of carbohydrate's ability to raise blood glucose levels) appear to increase insulin demand and accentuate hyperinsulinemia (6,7). However, there are few prospective studies addressing the association between diet and risk of NIDDM (2,7,8). To address further the hypothesis that diets with a high glycemic response and low cereal fiber content would influence the incidence of NIDDM, we examined prospectively the relationship between specific dietary patterns and risk of NIDDM in a cohort of 42,759 men while controlling for the major known risk factors.

RESEARCH DESIGN AND METHODS

Study population
The Health Professionals Follow-up Study is a national longitudinal study of diet and lifestyle factors in relation to chronic diseases among 51,529 U.S. male dentists, veterinarians, pharmacists, optometrists, osteopaths, and podiatrists who were 40–75 years of age in 1986; 95% of men were white (10). The participants returned a mailed questionnaire in 1986 concerning diet, medical history, and medications. Excluded from the analysis were the men who did not satisfy the a priori criteria of daily caloric intake between 800 and 4,200 kcal or of leaving more than 70 blanks out of the 131 total food items in the diet questionnaire (n = 1,595); fewer than 5% had more than 11 blanks. We also excluded men who reported in 1986 diabetes, cancer (except nonmelanoma skin cancer), myocardial infarction, angina, stroke, and coronary artery surgery because they may have modified their diet after the diagnosis (n = 7,175). One or more of these exclusions were met by 8,770 participants, leaving 42,759 eligible men who were followed for NIDDM incidence during the subsequent 6 years (1986–1992).

Dietary assessment
To assess participants' diets, we used a validated semiquantitative food-frequency questionnaire containing 131 food items and beverages plus vitamin supplements (11,12). We derived for each participant an average dietary glycemic index value. The glycemic index is a method of ranking foods on the basis of the incremental glucose response and insulin demand they produce for a given amount of carbohydrate (13,14). As suggested by Wolever et al. (15), we calculated the average dietary glycemic index for each participant by summing the products of the carbohydrate content per serving for each food times the average number of servings of that food per day, times its glycemic index, all divided by the total amount of carbohydrate daily intake. Following a similar principle, but without dividing by the total amount of carbohydrate, we also derived a score for the global dietary glycemic load as an indi-

Table 1—*Means of dietary intakes and other risk factors for NIDDM by quintile of energy-adjusted glycemic index score in a population of 42,759 U.S. men aged 40–75 years in 1986*

	Glycemic index quintiles (means)				
	1 (65.1)	2 (69.7)	3 (72.6)	4 (75.3)	5 (79.3)
Dietary factors (daily intake)					
Total calories (kcal)	1,960	2,010	2,016	2,016	1,971
Carbohydrate (g/day)	222	231	236	239	244
Vegetable fat (g/day)	29.0	29.5	30.3	30.7	31.5
Animal fat (g/day)	42.3	41.6	41.4	41.2	40.4
Protein (g/day)	95	94	92	90	87
Dietary fiber (g/day)	20.8	21.5	21.2	20.6	20.0
Cereal fiber (g/day)	4.5	5.6	6.0	6.2	6.9
Alcohol (g/day)	17.5	13.0	11.1	9.9	8.0
Magnesium (mg/day)	386	369	355	338	320
Foods (servings per week)					
Cooked potatoes	1.5	2.0	2.2	2.4	2.7
French frieds potatoes	0.5	0.6	0.7	0.9	1.0
Cola beverages	0.6	0.8	1.1	1.4	1.9
Other carbonated beverages	0.3	0.4	0.5	0.6	0.7
Jams	1.5	2.0	2.1	2.1	2.1
Pasta	1.0	1.1	1.2	1.1	1.0
White bread	1.9	2.6	3.2	4.2	6.1
English muffins	0.8	1.1	1.3	1.5	1.8
White rice	0.6	0.8	0.9	1.0	1.3
Cold breakfast cereal	1.8	2.4	2.8	3.0	3.7
Physical activity (METs/day)	21.1	21.4	20.4	19.1	17.3
BMI (kg/m^2)	25.7	25.5	25.5	25.4	25.3
Current smokers (%)	14.4	9.8	8.7	8.9	8.7
Family history NIDDM (%)	16.6	16.9	17.0	17.5	17.8

Data were directly standardized to the age and BMI distribution of the entire study group, except BMI, which was only age-standardized. METs, metabolic equivalents.

cator of a glucose response or insulin demand induced by the total carbohydrate intake. For both previous calculations, we used published data for glycemic index values (16,17) and the carbohydrate content in each serving reported by the U.S. Department of Agriculture (18). To control for total energy intake, all nutrients as well as the glycemic index and glycemic load variables were adjusted for total energy using the residuals method (19).

Measurement of nondietary factors
In 1986, participants provided information on their age, weight, height, and smoking status (20). Physical activity in metabolic equivalents per week was computed using the duration per week of various forms of exercise, weighting each activity by its intensity level (21). In 1987, participants provided information on history of NIDDM in 1st degree relatives.

Follow-up and ascertainment of cases
On follow-up questionnaires mailed every 2 years (in 1988, 1990, and 1992), we inquired whether diabetes had been newly diagnosed. We mailed to participants reporting NIDDM a supplementary questionnaire to ascertain the date and procedure of diagnosis, as well as clinical data and treatment. We met the criteria of NIDDM proposed by the National Diabetes Data Group (22) and the World Health Organization (23); the validity of this procedure has been previously documented (2).

Statistical analysis
For each participant, person-months of follow-up were counted from the date of return of the 1986 questionnaire to the date of diabetes diagnosis, to death or to January 31, 1992, whichever came first. Relative risks were estimated as odds ratios using a logistic regression analysis (24). We tested for monotonic trends with increasing levels of dietary factors by median values for each quintile category, modeling these as a continuous variable in logistic regression models. All P values are two-sided.

RESULTS — Among the baseline population of 42,759 men, the dietary glycemic index was positively associated with carbohydrate and cereal fiber intake, and it was negatively associated with the consumption of magnesium, alcohol, and animal fat (Table 1). The glycemic index was also positively associated with the frequency of intake of most foods contributing to total carbohydrate variation in our cohort (Table 1). A similar pattern of association was observed with the glycemic load score.

We documented 523 incident cases of NIDDM during a 6-year follow-up period (1986–1992). Total energy intake was not related to risk of NIDDM after adjustment for age, obesity, physical activity, alcohol consumption, smoking, and family history of NIDDM. Animal fat intake was not associated with risk of NIDDM, and vegetable fat was inversely associated with risk of NIDDM, although this was not statistically significant (Table 2). Dietary total fat, saturated, monounsaturated, and polyunsaturated fat were not appreciably associated with risk of NIDDM (Table 2), nor was the polyunsaturated/saturated fat ratio.

Total dietary fiber was not associated with a significant reduction in risk of NIDDM. However, cereal fiber had a significant inverse association with risk of NIDDM, while fruit and vegetable fiber did not (Table 3). The association with cereal fiber was observed also after adjustment for other fiber sources. Magnesium, calcium, and potassium were all inversely related to risk of NIDDM, but only for magnesium was the trend statistically significant (Table 3).

Total carbohydrate intake was not related to risk of NIDDM, whereas the glycemic index was positively associated with risk, although this relationship became statistically significant only after adjustment for cereal fiber intake (Table 4). The glycemic load score was not related to risk of NIDDM in the basic model, but when adjusted for cereal fiber intake the glycemic load became positively associated, although the test for trend was not statistically significant. We observed a synergistic relation between glycemic load and cereal fiber intake when we cross-classified participants by both variables. The relative risk was 2.17 (CI 1.04–4.54) for the combination of a high glycemic load and a low cereal fiber intake compared with the opposite extreme (Fig. 1). The test for interaction between the glycemic load and the cereal fiber intake was significant ($P <$ 0.001) in a logistic model that included

Table 2—*Adjusted relative risk of NIDDM by quintile of total energy and energy-adjusted fat intake in a population of 42,759 U.S. men aged 40–75 years in 1986, followed for 6 years*

| | Quintile | | | | | P value |
	1	2	3	4	5	for trend
Total energy intake, RR (95% CI)	1.0	1.00 (0.75–1.33)	1.24 (0.94–1.64)	1.12 (0.84–1.49)	1.22 (0.92–1.61)	0.13
Median intake (kcal/day)	1249	1606	1902	2245	2831	
NIDDM (n)	97	95	113	102	116	
Vegetable fat, RR (95% CI)	1.0	0.95 (0.73–1.24)	0.95 (0.72–1.25)	0.99 (0.75–1.30)	0.83 (0.62–1.11)	0.28
Median intake (g/day)	18.5	24.5	29.1	34.0	42.6	
NIDDM (n)	113	109	103	107	91	
Animal fat, RR (95% CI)	1.0	0.89 (0.64–1.25)	1.19 (0.87–1.62)	1.19 (0.88–1.62)	1.11 (0.82–1.50)	0.26
Median intake (g/day)	26.5	34.5	49.5	47.0	57.3	
NIDDM (n)	67	76	110	129	141	
Saturated fat, RR (95% CI)	1.0	1.20 (0.87–1.65)	1.31 (0.96–1.78)	1.17 (0.85–1.59)	1.03 (0.75–1.41)	0.75
Median intake (g/day)	16.7	21.3	24.3	27.3	32.1	
NIDDM (n)	66	97	119	119	122	
Polyunsaturated fat, RR (95% CI)	1.0	1.00 (0.76–1.34)	1.00 (0.76–1.34)	1.16 (0.89–1.54)	1.01 (0.77–1.35)	0.70
Median intake (g/day)	9.2	11.3	12.8	14.5	17.4	
NIDDM (n)	100	101	102	116	104	
Monounsaturated fat, RR (95% CI)	1.0	1.04 (0.76–1.42)	1.26 (0.93–1.69)	1.16 (0.85–1.56)	1.01 (0.74–1.37)	0.96
Median intake (g/day)	19.5	24.2	27.3	30.2	36.6	
NIDDM (n)	73	89	119	120	122	

Adjusted for age (40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70+ years); BMI (<23, 23, 24, 25–26, 27–28, 29–30, 31–32, 33–34, >35 kg/m², missing information); alcohol intake (no drinkers, 0.1–4.9, 5–9.9, 10–14.9, 15–29.9, 30–49.9 and >50 g/day); smoking status (never, past, 15–24 cig/day, 25+ cig/day, missing information); physical activity (quintiles of METs) and family history of diabetes (yes, no).

both main effect terms as well as the cross-product term of high glycemic load and low cereal fiber. We created a dichotomous variable comparing men with low cereal fiber intake and high glycemic load (the elevated group in Fig. 1) to all others to represent the combined effect of these variables (RR = 1.69, 95% CI 1.14–2.47). This association remained significant when magnesium was included in the same model as a continuous variable (RR = 1.57, 95% CI 1.07–2.32) as did the inverse rela-

Table 3—*Adjusted relative risk of NIDDM by quintile of energy-adjusted total carbohydrate, dietary fiber, and magnesium intake in a population of 42,759 U.S. men aged 40–75 years in 1986, followed for 6 years*

| | Quintile | | | | | P value |
	1	2	3	4	5	for trend
Total carbohydrate, RR (95% CI)	1.0	0.88 (0.67–1.14)	0.93 (0.71–1.22)	0.88 (0.66–1.17)	0.85 (0.62–1.15)	0.33
Median intake (g/day)	182	213	234	255	288	
NIDDM (n)	132	112	107	93	79	
Total dietary fiber, RR (95% CI)	1.0	0.98 (0.75–1.29)	1.08 (0.83–1.42)	0.87 (0.65–1.17)	0.98 (0.73–1.33)	0.70
Median intake (g/day)	13.4	17.1	20.0	23.5	29.7	
NIDDM (n)	114	109	118	92	90	
Cereal fiber, RR (95% CI)	1.0	1.14 (0.89–1.46)	0.95 (0.73–1.25)	0.91 (0.69–1.20)	0.70 (0.51–0.96)	0.007
Median intake (g/day)	2.5	3.8	5.0	6.8	10.2	
NIDDM (n)	127	136	102	95	63	
Fruit fiber, RR (95% CI)	1.0	1.01 (0.76–1.34)	0.89 (0.67–1.19)	1.14 (0.86–1.51)	1.01 (0.76–1.36)	0.68
Median intake (g/day)	1.2	2.8	3.8	5.3	8.3	
NIDDM (n)	106	104	95	119	101	
Vegetable fiber, RR (95% CI)	1.0	1.12 (0.85–1.49)	1.22 (0.93–1.61)	1.10 (0.83–1.46)	1.12 (0.84–1.49)	0.65
Median intake (g/day)	3.5	4.9	6.3	7.9	11.3	
NIDDM (n)	96	104	118	103	102	
Magnesium, RR (95% CI)	1.0	0.92 (0.72–1.19)	0.83 (0.64–1.08)	0.66 (0.49–0.88)	0.72 (0.54–0.96)	0.004
Median intake (mg/day)	262	307	343	385	461	
NIDDM (n)	132	122	107	80	82	

Adjusted for age (40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70+ years); BMI (<23, 23, 24, 25–26, 27–28, 29–30, 31–32, 33–34, >35 kg/m², missing information); alcohol intake (no drinkers, 0.1–4.9, 5–9.9, 10–14.9, 15–29.9, 30–49.9 and >50 g/day); smoking status (never, past, 15–24 cig/day, 25+ cig/day, missing information); physical activity (quintiles of METs) and family history of diabetes (yes, no).

Table 4—*Adjusted relative risk of NIDDM by quintile of the energy-adjusted glycemic index and glycemic load score when adding to the basic model other potential dietary confounders*

| | Quintile | | | | | P value |
	1	2	3	4	5	for trend
Glycemic index						
Quintile median	65	70	73	75	79	
NIDDM (n)	99	107	105	103	109	
Person-years (n)	46,592	46,971	47,001	46,815	46,338	
Basic model, RR (95% CI)	1.0	1.14 (0.86–1.50)	1.13 (0.85–1.50)	1.14 (0.86–1.51)	1.27 (0.96–1.69)	0.12
Further adjusted for cereal fiber intake, RR (95% CI)	1.0	1.16 (0.88–1.50)	1.19 (0.89–1.58)	1.20 (0.90–1.60)	1.37 (1.02–1.83)	0.03
Glycemic load						
Quintile median	119	144	160	177	203	
NIDDM (n)	120	120	103	93	87	
Person-years (n)	46,786	47,215	47,425	46,830	45,460	
Basic model, RR (95% CI)	1.0	1.04 (0.80–1.36)	0.97 (0.73–1.28)	1.01 (0.75–1.36)	1.05 (0.77–1.43)	0.83
Further adjusted for cereal fiber intake, RR (95% CI)	1.0	1.07 (0.82–1.41)	1.04 (0.78–1.39)	1.13 (0.83–1.54)	1.25 (0.90–1.73)	0.17

Adjusted for age (40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70+ years); BMI (<23, 23, 24, 25–26, 27–28, 29–30, 31–32, 33–34, >35 kg/m², missing information); alcohol intake (no drinkers, 0.1–4.9, 5–9.9, 10–14.9, 15–29.9, 30–49.9 and >50 g/day); smoking status (never, past, 15–24 cig/day, 25+ cig/day, missing information); physical activity (quintiles of METs) and family history of diabetes (yes, no).

tionship with magnesium (*P* = 0.003).

We also examined the relationship between the 20 foods contributing most to variation of carbohydrate consumption within our cohort. We observed significant inverse associations with cold breakfast cereal and yogurt; and significant positive associations with carbonated beverages, white bread, white rice, and french fried potatoes.

CONCLUSIONS — Our results suggest that the diets with high glycemic load and low cereal fiber content are positively associated with risk of NIDDM, independent of other currently known risk factors. The prospective design of this study avoids the possibility of biased recall of diet because all data on food intake were collected before the diagnosis of NIDDM. In our study, self-reported diabetes was confirmed by a supplementary questionnaire, and some men may have asymptomatic undiagnosed NIDDM. However, underdiagnosis would tend to lead to an underestimate of the true association between dietary factors and diabetes. We also considered the possibility that men with unhealthy diets were more likely to have screening for diabetes. However, the proportion of asymptomatic cases did not vary appreciably by level of glycemic load score, magnesium, or dietary fiber intake.

Previous prospective studies (2,8,9) as well as the present analysis have consistently found little relationship between total

carbohydrate intake and risk of NIDDM. Using total carbohydrate intake, however, does not take into account the glycemic effect or insulin demand of various forms of carbohydrates. Metabolic studies have documented differences in insulin demand generated by various foods, depending largely on the type or degree of digestibility of the starch content (13,17). The carbohydrates in starchy foods with a low glycemic

index have been called lente-carbohydrates (25), which are mainly from less processed grain products and dried legumes that maintain their original fiber content. To evaluate the relationship between carbohydrate intake and risk of NIDDM, we examined the quality as well as the quantity of carbohydrates consumed. The glycemic index, as a relative measure of glycemic response to a given amount of carbohy-
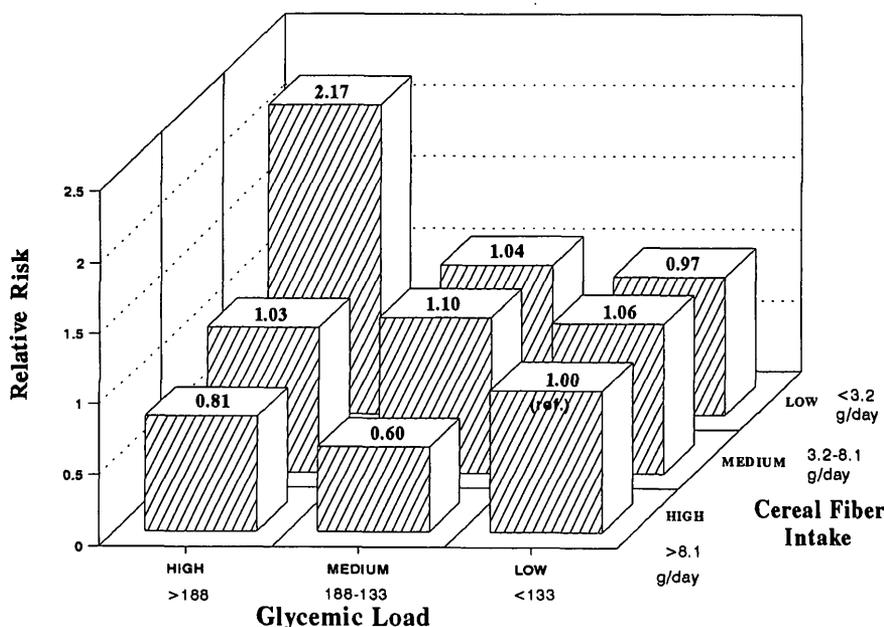

Figure 1—*Relative risk of NIDDM by different levels of cereal fiber intake and glycemic load.*

drate, does describe the quality of carbohydrate but does not take into account the quantity. In contrast, the total glycemic load represents the combination of quality as well as the quantity of carbohydrate.

In some metabolic studies among patients with NIDDM, high-fiber diets have decreased insulin demand (4,5). The type of fiber may be differentially related to risk of NIDDM and the amount of dietary fiber consumed may modify the insulin demand that other foods generate (26). However, there are sparse epidemiological data on the relationship between different types of dietary fiber intake and the incidence of NIDDM, and on the potential interactions with other dietary factors (2). In our present study, total dietary fiber was only weakly related with risk of NIDDM, but fiber from cereals had an inverse independent relationship to risk of NIDDM.

Hyperinsulinemia, a manifestation of insulin resistance, is one of the best predictors of NIDDM and populations at high risk of NIDDM have higher insulin levels (27). Diets with a high glycemic index increase insulin demand and hyperinsulinemia in patients with NIDDM (6). Therefore, diets with a high glycemic load and low cereal fiber are likely to lead to a chronic high demand for insulin, which may be exacerbated by insulin resistance. As long as the pancreas is able to augment insulin secretion to meet the extra demand, glucose tolerance remains normal. But if the endocrine pancreas fails to respond adequately (relative insulin deficiency), glucose intolerance ensues, eventually leading to NIDDM (28).

Metabolic studies suggest an inverse association between intracellular magnesium and insulin resistance (29). A beneficial effect of magnesium supplementation on insulin sensitivity in patients with NIDDM (30) and in normal subjects (31) has also been established in small clinical trials. In a previous analysis of the Nurses' Health Study (2) and in our present analysis, we observed an independent inverse association between magnesium intake and risk of NIDDM.

Beyond the well-known risk factors for NIDDM of age, obesity, family history, sedentary lifestyle, and smoking, our findings support the hypotheses that diets with high glycemic load and low cereal fiber consumption increase risk of NIDDM in men, particularly when consumed in combination. Our findings also suggest that magnesium may contribute to lower risk associated

with the consumption of whole grain foods. These findings suggest that grains should be consumed in a minimally refined form to reduce the incidence of diabetes.

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