Dietary Fiber, Glycemic Load, and Risk of Non–insulin-dependent Diabetes Mellitus in Women

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Objective.—To examine prospectively the relationship between glycemic diets, low fiber intake, and risk of non–insulin-dependent diabetes mellitus.

Design.—Cohort study.

Setting.—In 1986, a total of 65 173 US women 40 to 65 years of age and free from diagnosed cardiovascular disease, cancer, and diabetes completed a detailed dietary questionnaire from which we calculated usual intake of total and specific sources of dietary fiber, dietary glycemic index, and glycemic load.

Main Outcome Measure.—Non–insulin-dependent diabetes mellitus.

Results.—During 6 years of follow-up, 915 incident cases of diabetes were documented. The dietary glycemic index was positively associated with risk of diabetes after adjustment for age, body mass index, smoking, physical activity, family history of diabetes, alcohol and cereal fiber intake, and total energy intake. Comparing the highest with the lowest quintile, the relative risk (RR) of diabetes was 1.37 (95% confidence interval [CI], 1.09-1.71; P trend=.005). The glycemic load (an indicator of a global dietary insulin demand) was also positively associated with diabetes (RR=1.47; 95% CI, 1.16-1.86; P trend=.003). Cereal fiber intake was inversely associated with risk of diabetes when comparing the extreme quintiles (RR=0.72, 95% CI, 0.58-0.90; P trend=.001). The combination of a high glycemic load and a low cereal fiber intake further increased the risk of diabetes (RR=2.50, 95% CI, 1.14-5.51) when compared with a low glycemic load and high cereal fiber intake.

Conclusions.—Our results support the hypothesis that diets with a high glycemic load and a low cereal fiber content increase risk of diabetes in women. Further, they suggest that grains should be consumed in a minimally refined form to reduce the incidence of diabetes.

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NON–INSULIN-DEPENDENT diabetes mellitus (NIDDM) is characterized by a decrease in the effect of insulin on peripheral tissues (insulin resistance) and by the inability of the endocrine pancreas to compensate for this resistance (relative insulin deficiency). Genetic factors, as well as age and obesity, have been described as the major risk factors for insulin resistance and NIDDM. Nevertheless, there has been great interest in the role of other potentially modifiable factors such as physical activity, smoking, and alcohol consumption. Particular attention has been focused on the hypothesis that dietary factors that increase insulin resistance or insulin demands would, over the long term, influence the risk of NIDDM.

In animal studies, saturated fat intake is directly related to insulin resistance; however, inconsistent results have been observed in clinical settings. In some clinical studies a beneficial effect of a high-fiber diet on insulin demand in NIDDM subjects has been suggested. Also, results from metabolic studies have suggested that carbohydrates with a high glycemic index (a qualitative indicator of carbohydrate’s ability to raise blood glucose levels) increase insulin demand and accentuate hyperinsulinemia. Recent analysis on the long-term effect of dietary patterns on insulin levels suggest that animal fat may increase insulin levels, whereas dietary fiber may decrease them. However, there are few prospective studies addressing the association between diet and risk of NIDDM, and some of them with methodologic limitations in measuring diet or incomplete control for obesity and other risk factors.

In an earlier analysis from the Nurses’ Health Study (1980-1986), we observed that magnesium intake was inversely associated with risk of NIDDM. In a recent analysis of a 6-year follow-up period in a parallel study among men, we found that intakes of cereal fiber and magnesium were inversely associated with risk of NIDDM and that consumption of carbohydrates with a high glycemic index was positively associated with risk of NIDDM.

To address further the hypothesis that diets leading to a high insulin demand would influence the risk of NIDDM, we examined prospectively the relationship between specific dietary patterns and risk of NIDDM in a cohort of 65 173 women while controlling for the major known risk factors for diabetes.

METHODS

Study Population

The Nurses’ Health Study is a longitudinal study of diet and lifestyle factors in relation to chronic diseases among 121 700 US female registered nurses aged 30 to 55 years at enrollment. The cohort was assembled in 1976 when the participants returned a mailed questionnaire about known and suspected risk factors for cancer and cardiovascular disease. In 1980, we assessed diet with a 61-item semiquantitative food frequency questionnaire. In 1986, an expanded food frequency questionnaire (134 food items) was mailed to cohort members. For the current analysis, we used information from respondents to the 1986 questionnaire, comprising 75 543 women aged 40 to 65 years; these data are thus independent of our earlier report. We excluded participants who did not satisfy the prior criteria of daily energy intake between 2512 and 14 654 kJ and those who left 10 or more blanks among the 134 total food items in the dietary questionnaire. In addition, women who reported on the 1986 or a previous questionnaire a diagnosis of diabetes mellitus, cancer (except nonmelanoma skin cancer), myocardial infarction, angina, stroke, and coronary artery surgery were also excluded, because they...
may have modified their diet after the diagnosis. One or more of the above reasons for exclusion were met by 10,370 participants, leaving 65,173 eligible women who were followed for NIDDM incidence in the subsequent 6 years (1986-1992).

**Dietary Assessment**

To assess the participants' diets, a validated semiquantitative food frequency questionnaire containing 134 food items and beverages as well as vitamin supplements was used in 1986. Nutrient scores were computed by multiplying the frequency of consumption of each unit of food derived from the food frequency questionnaire by the nutrient content of the specified portion size according to the food composition tables from the US Department of Agriculture. A full description of the food frequency questionnaire in its abbreviated form (61 items) and of the procedures for calculation of nutrient intake, as well as data on reproducibility and validity in this cohort, have been previously reported. Data on reproducibility and validity of the 134-item food frequency questionnaire used in a parallel study of men have been previously reported (energy-adjusted mean daily intake).

**Measurement of Nondietary Factors**

In 1982, the participants provided information on history of diabetes in first-degree relatives. In 1986 the participants provided information on their weight and smoking status. The validity of self-reported weight in this cohort has been reported previously (correlation coefficient of 0.96 between self-reported and measured weight). The level of physical activity in metabolic equivalents per week was estimated based on self-reported duration per week of various forms of exercise, weighting each activity by its intensity level.

**Follow-up andAscertainment of Cases**

On follow-up questionnaires mailed every 2 years (1988, 1990, and 1992) we inquired whether diabetes had been newly diagnosed. When diabetes mellitus was reported on a follow-up questionnaire, we mailed the participant a supplementary questionnaire to confirm the report and to ascertain the date of diagnosis, tests done to confirm the diagnosis, presenting symptoms, and medications. The diagnosis of NIDDM was established whenever 1 or more of the following criteria were met: (1) 1 or more classic symptoms (thirst, polyuria, weight loss, pruritus), plus a fasting plasma glucose concentration of 7.8 mmol/L (140 mg/dL) or higher or a random plasma glucose concentration of 11.1 mmol/L (200 mg/dL) or higher; or (2) at least 2 elevated plasma glucose concentrations on different occasions (fasting ≥ 7.8 mmol/L [140 mg/dL] and/or random ≥ 11.1 mmol/L [200 mg/dL] after 2 hours or more on oral glucose tolerance testing) in the absence of symptoms; or (3) treatment with hypoglycemic medication (insulin or oral hypoglycemic agents). These criteria correspond to those proposed by the National Diabetes Data Group and the World Health Organization.

The glycemic index was also positively related to the frequency of intake of the foods contributing to carbohydrate variation intake in our cohort (Table 1). A similar pattern of association was observed with the glycemic load score.

We documented 915 incident cases of NIDDM during a 6-year follow-up period (1986-1992). Total energy intake was weakly and positively related to risk of NIDDM after adjustment for age, obesity, alcohol consumption, smoking, physical activity, and family history, although the test for trend was not statistically significant (Table 2). Animal fat intake

**RESULTS**

Among the baseline population of 65,173 women, the dietary glycemic index was positively associated with carbohydrate and cereal fiber intake and negatively associated with consumption of magnesium, alcohol, and animal fat (Table 1). The glycemic index was also positively related to the frequency of intake of the foods contributing to carbohydrate variation intake in our cohort (Table 1). A similar pattern of association was observed with the glycemic load score.

We documented 915 incident cases of NIDDM during a 6-year follow-up period (1986-1992). Total energy intake was weakly and positively related to risk of NIDDM after adjustment for age, obesity, alcohol consumption, smoking, physical activity, and family history, although the test for trend was not statistically significant (Table 2). Animal fat intake...
was unrelated with risk of NIDDM, whereas vegetable fat was inversely associated with risk of NIDDM, although it was not statistically significant. Dietary monounsaturated and polyunsaturated fat were not appreciably associated with risk of NIDDM (Table 2), nor was the ratio of polyunsaturated to saturated fat.

We observed a significant inverse association between total dietary fiber intake and risk of NIDDM. Among the different sources of dietary fiber, cereal fiber was inversely associated with risk of NIDDM, whereas fruit and vegetable fiber were not clearly related to risk (Table 3). Magnesium, calcium, and potassium were inversely related to risk of NIDDM, but only for magnesium was the trend significant (Table 3). The inverse association with magnesium remained significant after further adjustment for cereal fiber intake and glycemic load.

Although total carbohydrate intake was not related to risk of NIDDM, both the glycemic index as well as the glycemic load score were positively associated with risk. However, the glycemic load score became significant only after adjustment for cereal fiber intake (Table 4).

We examined the joint effect of the glycemic load and the cereal fiber intake by cross-classifying participants by both variables. The RR for the combination of a high glycemic load and a low cereal fiber intake compared with the opposite extreme was 2.50 (confidence interval [CI], 1.14-5.51) (Figure).

We also examined the relation to risk of NIDDM of the 20 foods contributing most to variation of carbohydrate consumption within this cohort. We observed significant inverse associations with cold breakfast cereal and yogurt, and significant positive associations with cola beverages, white bread, white rice, of NIDDM, and cooked potatoes.

In the main results we further included in the basic model waist-hip ratio as a covariate; however, the results did not change after controlling for waist-hip ratio. We also repeated our analysis adjusting for updated values from the biennial

Table 1—Means of Dietary Intakes and Other Risk Factors for Non-insulin-dependent Diabetes (NIDDM) by Quintile of Energy-Adjusted Glycemic Index Score in a Population of 85 173 US Women Aged 40 to 65 Years in 1986*  

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Quintile (Mean)</th>
<th>1 (62.9)</th>
<th>2 (66.1)</th>
<th>3 (70.7)</th>
<th>4 (73.4)</th>
<th>5 (77.9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total energy intake, kJ/d</td>
<td>7253</td>
<td>7363</td>
<td>7594</td>
<td>7531</td>
<td>7106</td>
<td></td>
</tr>
<tr>
<td>Carbohydrate, g/d</td>
<td>184</td>
<td>191</td>
<td>193</td>
<td>196</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td>Protein, g/d</td>
<td>79</td>
<td>77</td>
<td>75</td>
<td>73</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Vegetable fat, g/d</td>
<td>23.7</td>
<td>24.7</td>
<td>25.4</td>
<td>25.0</td>
<td>26.7</td>
<td></td>
</tr>
<tr>
<td>Animal fat, g/d</td>
<td>34.0</td>
<td>32.9</td>
<td>32.5</td>
<td>32.2</td>
<td>31.7</td>
<td></td>
</tr>
<tr>
<td>Dietary fiber, g/d</td>
<td>17.4</td>
<td>18.0</td>
<td>17.8</td>
<td>17.6</td>
<td>17.1</td>
<td></td>
</tr>
<tr>
<td>Cereal fiber, g/d</td>
<td>3.6</td>
<td>4.3</td>
<td>4.5</td>
<td>4.7</td>
<td>5.1</td>
<td></td>
</tr>
<tr>
<td>Alcohol, g/d</td>
<td>9.4</td>
<td>7.2</td>
<td>6.0</td>
<td>5.3</td>
<td>4.3</td>
<td></td>
</tr>
<tr>
<td>Magnesium, mg/d</td>
<td>321</td>
<td>313</td>
<td>301</td>
<td>289</td>
<td>271</td>
<td></td>
</tr>
</tbody>
</table>

Table 2—Adjusted Relative Risk (RR) of Non-insulin-dependent Diabetes (NIDDM) by Quintile of Total Energy Intake and Energy-Adjusted Fat Intake in a Population of 85 173 US Women Aged 40 to 65 Years in 1986, Followed Up for 6 Years*  

**Adjusted for age (40-44, 45-49, 50-54, 55-59, and 60-65 years), body mass index (BMI) (23, 24, 25-26, 27-28, 29-30, 31-32, 33-34, >35 kg/m², and missing information), alcohol intake (no drinkers, 0.1-0.4, 0.5-0.9, 1.0-1.4, 1.5-2.0, 2.1-2.5, 2.6-3.0, 3.1-3.5, 3.6-4.0, >4.0 g/d), smoking status (never, past, 1-14, 15-24, >25 cigarettes per day, and missing information), physical activity (quintiles of metabolic equivalents), and family history of diabetes (yes or no). CI indicates confidence interval.

†Reference quintile.
follow-up questionnaires for those variables in the basic model; again no appreciable changes were observed.

**COMMENT**

In this large-scale prospective study, we observed that diets with high glyce-mic load and low cereal fiber content were positively associated with risk of NIDDM, independent of other dietary factors and 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. Incomplete follow-up is unlikely to distort these results since the follow-up rate was over 90% and similar for each level of baseline of the dietary variables. We considered the possibility that a diagnostic bias might account for the observed relationship between dietary intake patterns and risk of NIDDM. It could be possible that women with unhealthy diets may be more likely to have screening tests for diabetes. However, the proportion of cases without reported symptoms at diagnosis did not vary appreciably by level of glycemic load score, magnesium or dietary fiber intake, nor did the frequency of physician visits within the first 2 years of follow-up. Further, when only cases who were symptomatic at diagnosis were considered, the association with glycemic load was even stronger than for all cases of NIDDM.

Previous prospective studies as well as the current 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 containing the same amount of carbohydrate, depending largely on the type or degree of digestibility of the starch content. Foods with a higher carbohydrate digestibility generate a higher insulin demand. The carbohyd-rate in starchy foods with a low glycemic index have been called lente carbohydrates, which are mainly from less processed grain products that maintain their original fiber content. Some representative values for food with low and high glycemic index are white bread, 100; dark bread, 58-70; mashed potatoes, 104;

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**Table 3.** Adjusted Relative Risk (RR) of Non–Insulin-Dependent Diabetes (NIDDM) by Quintile of Energy-Adjusted Carbohydrate, Dietary Fiber, and Magnesium Intake in a Population of 65,173 US Women Aged 40 to 65 Years in 1986, Followed Up for 6 Years

<table>
<thead>
<tr>
<th>Quintile</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total carbohydrate, RR (95% CI)</td>
<td>1.0</td>
<td>0.94 (0.76-1.17)</td>
<td>1.14 (0.92-1.41)</td>
<td>0.96 (0.76-1.21)</td>
<td>1.04 (0.83-1.30)</td>
<td>.83</td>
</tr>
<tr>
<td>Median intake, g/d</td>
<td>155</td>
<td>178</td>
<td>189</td>
<td>200</td>
<td>231</td>
<td></td>
</tr>
<tr>
<td>Cases of NIDDM, No.</td>
<td>177</td>
<td>174</td>
<td>209</td>
<td>189</td>
<td>165</td>
<td></td>
</tr>
<tr>
<td>Total dietary fiber, RR (95% CI)</td>
<td>1.0</td>
<td>1.01 (0.83-1.24)</td>
<td>0.90 (0.73-1.11)</td>
<td>0.91 (0.74-1.13)</td>
<td>0.78 (0.62-0.98)</td>
<td>.02</td>
</tr>
<tr>
<td>Median intake, g/d</td>
<td>11.8</td>
<td>14.7</td>
<td>17.0</td>
<td>19.6</td>
<td>24.1</td>
<td></td>
</tr>
<tr>
<td>Cases of NIDDM, No.</td>
<td>192</td>
<td>203</td>
<td>179</td>
<td>188</td>
<td>153</td>
<td></td>
</tr>
<tr>
<td>Fruit fiber, RR (95% CI)</td>
<td>1.0</td>
<td>0.87 (0.70-1.07)</td>
<td>0.95 (0.77-1.18)</td>
<td>0.94 (0.76-1.16)</td>
<td>0.87 (0.70-1.08)</td>
<td>.39</td>
</tr>
<tr>
<td>Median intake, g/d</td>
<td>1.4</td>
<td>2.6</td>
<td>3.7</td>
<td>5.1</td>
<td>7.6</td>
<td></td>
</tr>
<tr>
<td>Cases of NIDDM, No.</td>
<td>168</td>
<td>187</td>
<td>192</td>
<td>182</td>
<td>182</td>
<td></td>
</tr>
<tr>
<td>Vegetable fiber, RR (95% CI)</td>
<td>1.0</td>
<td>1.40 (1.13-1.73)</td>
<td>1.23 (0.99-1.53)</td>
<td>1.29 (1.04-1.61)</td>
<td>1.17 (0.93-1.46)</td>
<td>.54</td>
</tr>
<tr>
<td>Median intake, g/d</td>
<td>3.4</td>
<td>4.8</td>
<td>5.9</td>
<td>7.2</td>
<td>9.6</td>
<td></td>
</tr>
<tr>
<td>Cases of NIDDM, No.</td>
<td>156</td>
<td>204</td>
<td>183</td>
<td>194</td>
<td>178</td>
<td></td>
</tr>
<tr>
<td>Cereal fiber, RR (95% CI)</td>
<td>1.0</td>
<td>1.01 (0.83-1.23)</td>
<td>0.85 (0.69-1.04)</td>
<td>0.82 (0.66-1.01)</td>
<td>0.72 (0.58-0.90)</td>
<td>.001</td>
</tr>
<tr>
<td>Median intake, g/d</td>
<td>2.0</td>
<td>2.9</td>
<td>3.7</td>
<td>4.9</td>
<td>7.5</td>
<td></td>
</tr>
<tr>
<td>Cases of NIDDM, No.</td>
<td>210</td>
<td>213</td>
<td>183</td>
<td>169</td>
<td>140</td>
<td></td>
</tr>
<tr>
<td>Magnesium, RR (95% CI)</td>
<td>1.0</td>
<td>0.91 (0.74-1.10)</td>
<td>0.84 (0.69-1.03)</td>
<td>0.82 (0.67-1.01)</td>
<td>0.62 (0.50-0.78)</td>
<td>.001</td>
</tr>
<tr>
<td>Median intake, mg/d</td>
<td>222</td>
<td>261</td>
<td>292</td>
<td>327</td>
<td>338</td>
<td></td>
</tr>
<tr>
<td>Cases of NIDDM, No.</td>
<td>224</td>
<td>201</td>
<td>180</td>
<td>179</td>
<td>131</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for age (40-44, 45-49, 50-54, 55-59, and 60-65 years), body mass index (<23, 23, 24, 25-26, 27-28, 29-30, 31-32, 33-34, ≥35 kg/m², and missing information), alcohol intake (no drinkers, 0.1-1.4, 1.5-2.9, 3.0-4.4, 5.5-10.4, 10.5-17.0, and ≥17.0 g/d), smoking status (never, past, 1-14, 15-24, ≥25 cigarettes per day, and missing information), physical activity (quintiles of metabolic equivalents), and family history of diabetes (yes or no). CI indicates confidence interval.

†Reference quintile.

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**Table 4.** Adjusted Relative Risk of Non–Insulin-Dependent Diabetes (NIDDM) by Quintile of the Energy-Adjusted Glycemic Index and Glycemic Load Score When Adding to the Basic Model Cereal Fiber Intake

<table>
<thead>
<tr>
<th>Glycemic index</th>
<th>Quintile</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quintile median</td>
<td>64</td>
<td>68</td>
<td>71</td>
<td>73</td>
<td>77</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td>Cases of NIDDM, No.</td>
<td>142</td>
<td>197</td>
<td>170</td>
<td>202</td>
<td>204</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic model, RR (95% CI)</td>
<td>1.0</td>
<td>1.16 (0.92-1.45)</td>
<td>1.29 (1.03-1.61)</td>
<td>1.28 (1.02-1.59)</td>
<td>1.25 (0.99-1.54)</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td>Further adjusted for cereal fiber intake, RR (95% CI)</td>
<td>1.0</td>
<td>1.21 (0.96-1.52)</td>
<td>1.37 (1.10-1.72)</td>
<td>1.37 (1.09-1.71)</td>
<td>1.37 (1.09-1.71)</td>
<td>.005</td>
<td></td>
</tr>
<tr>
<td>Glycemic load</td>
<td>Quintile median</td>
<td>111</td>
<td>131</td>
<td>144</td>
<td>157</td>
<td>178</td>
<td>. . .</td>
</tr>
<tr>
<td>Cases of NIDDM, No.</td>
<td>156</td>
<td>185</td>
<td>189</td>
<td>179</td>
<td>206</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic model, RR (95% CI)</td>
<td>1.0</td>
<td>1.17 (0.94-1.46)</td>
<td>1.11 (0.89-1.39)</td>
<td>1.11 (0.89-1.39)</td>
<td>1.26 (1.00-1.57)</td>
<td>.09</td>
<td></td>
</tr>
<tr>
<td>Further adjusted for cereal fiber intake, RR (95% CI)</td>
<td>1.0</td>
<td>1.24 (0.99-1.55)</td>
<td>1.22 (0.97-1.54)</td>
<td>1.25 (0.99-1.59)</td>
<td>1.47 (1.16-1.86)</td>
<td>.003</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for age (40-44, 45-49, 50-54, 55-59, and 60-65 years), body mass index (<23, 23, 24, 25-26, 27-28, 29-30, 31-32, 33-34, ≥35 kg/m², and missing information), alcohol intake (no drinkers, 0.1-1.4, 1.5-2.9, 3.0-4.4, 5.5-10.4, 10.5-17.0, and ≥17.0 g/d), smoking status (never, past, 1-14, 15-24, ≥25 cigarettes per day, and missing information), and family history of diabetes (yes or no). CI indicates confidence interval.

†Reference quintile.
cold breakfast cereal (depending on the type), 72-127; cola beverages, 87; apples, 65; orange juice, 65; yogurt, 35; broccoli, 45; and peanut butter, 40.50-52 To evaluate the relationship between carbohydrate intake and risk of NIDDM, it therefore seems critical to examine 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 carbohydrate, does represent 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 consumed, and may be interpreted as a measure of dietary insulin demand.

An extensive literature has addressed the link between consumption of fiber-depleted diets and the occurrence of several chronic diseases, including NIDDM. In some metabolic studies among patients with NIDDM, high-fiber diets have decreased insulin demand.53-57 It has also been suggested that the type of fiber could be differentially related to risk of NIDDM,58-60 and that the amount of dietary fiber consumed may modify the insulin demand that different foods generate; starchy foods mixed with viscous soluble fibers (guar gum) present lower glycemic responses than when eaten without it.50,61 However, there are sparse epidemiologic 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. In our current analysis, we found that total dietary fiber was inversely related with risk of NIDDM, but fiber from cereals had an especially strong inverse independent relationship to risk of NIDDM. Our results also suggest a particularly adverse effect of high glycemic load in combination with a low cereal fiber intake; the RR observed for this combination (RR = 2.50) was more than 2-fold greater relative to consumption of a diet high in cereal fiber and low in glycemic load. A similar pattern was observed in a parallel cohort of men.61

Hyperinsulinemia, a manifestation of insulin resistance, is 1 of the best predictors of NIDDM67-70 and populations at high risk of NIDDM have higher insulin levels.71 Diets with a high glycemic index increase insulin demand and hyperinsulinemia among patients with NIDDM,71 as well as in normal subjects.72 Therefore, diets with a high glycemic load as well as low cereal fiber content 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, leading to NIDDM.73-75 Why pancreatic "exhaustion" occurs is not clear, but it may be related to the effect of glucose toxicity in a genetically predisposed beta cell; in early stages, however, this pancreatic deficiency may be reversible.75-77

Metabolic studies suggest an inverse association between intracellular magnesium and insulin resistance.78,79 Also, a beneficial effect of magnesium supplementation on insulin sensitivity in patients with NIDDM80,81 and in normal subjects82 has been established in small clinical trials. Our results suggest that magnesium may be an independent predictor of NIDDM. The inverse relationship between dietary magnesium intake and risk of NIDDM we observed is consistent with our results of an earlier analysis in the Nurses' Health Study15 and a parallel study in men.83 However, in neither of these studies did we observe a consistent relationship between magnesium and NIDDM among the different food sources of magnesium, as would be expected for a true causal relationship. The high correlation between cereal fiber and magnesium may not permit a clear separation of the independent effect of magnesium from that of cereal fiber intake.

Most prospective studies exploring the relation between diet and NIDDM have not found a positive association between total fat intake and incidence of NIDDM. Our findings in the first 6-year follow-up period in the Nurses' Health Study15 and in a parallel study in men18 are consistent with our current results, suggesting that overall fat intake is not associated with risk of NIDDM.

Beyond the well-known risk factors for NIDDM of age, obesity, family history, sedentary lifestyle, and smoking, our findings support the hypothesis that a diet with high glycemic load and a low cereal fiber content increases risk of NIDDM. These findings suggest that grains should be consumed in a minimally refined form to reduce the incidence of diabetes.

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