Can Diabetes Be Prevented by Vegetable Fat?

The prevention of type 2 diabetes has become an important clinical and health policy issue around the globe because of the increasing rates of diabetes in developed as well as in developing countries. Evidence of successful programs concerning the primary prevention of diabetes has only very recently been provided. The Finnish Diabetes Prevention Study (1) was the largest randomized intervention study, which included 522 middle-aged overweight subjects with impaired glucose tolerance. The intervention consisted of individual counseling on reducing body weight, total fat intake, and intake of saturated fatty acids (SFAs) and increasing fiber intake and physical activity. After 4 years, the cumulative diabetes incidence was 11 vs. 23% in the control group. After 4 years, the cumulative diabetes incidence was 11 vs. 23% in the control group (P < 0.001). The reduction in diabetes was highest in the group with the largest changes in lifestyle.

An important feature of this study is that it resulted in a substantial decrease in diabetes risk despite an only modest difference in body weight (3 kg), which shows that other parts of the intervention played a role as well.

In this light, it is worthwhile to pay close attention to the role of dietary composition in diabetes etiology. In this issue of "Diabetes Care," Meyer et al. (2) report on the impact of various dietary fatty acids on the risk of type 2 diabetes in the Iowa Women’s Health Study. They studied 35,988 women, aged 55–69 years, free of diabetes, and followed them for 11 years, resulting in 1,890 new cases of type 2 diabetes. Intake of fat and fatty acids was assessed from a validated food-frequency questionnaire. After adjustments for main risk factors, including BMI, waist-to-hip ratio, physical activity, dietary fiber, magnesium, and other dietary fat subtypes, substituting polyunsaturated fatty acid (PUFA) intake for SFA was inversely associated with diabetes risk, with a 16% reduction in the highest quintile (median intake 16.6 g per day). The consumption of vegetable fat was associated with a 22% reduction in new cases of diabetes in the highest quintile (median 41.7 g per day).

Other nutrients that have been implicated in the prevention of diabetes, such as vitamin E, cannot explain the vegetable fat finding. Results were similar for overweight and normal-weight women.

This study can be well compared with the most recent results from the Nurses’ Health Study reported by Salmeron et al. (3). With a similar design and a similar food-frequency questionnaire, they followed a cohort of younger women (34–59 years of age) for 14 years. They observed a similar inverse association between diabetes risk and intake of vegetable fat and PUFAs, which strengthens the observations of Meyer et al. (2). Other similar findings are the absence of clear associations with SFA and monounsaturated fatty acid (MUFA) intake but a positive association with dietary cholesterol. In contrast, trans–fatty acid intake is associated with increased diabetes risk in the Nurses’ Health Study but not in the Iowa Women’s Health Study. In the Iowa Women’s Health Study, no indication of a beneficial effect of n-3 PUFA (mostly from fish) on diabetes risk was observed, whereas in the Nurses’ Health Study, a reduced diabetes risk was observed in the highest one-fifth of intake (relative risk 0.8).

Results of earlier epidemiological studies of various designs have been previously summarized (4). Inverse associations with intake of PUFAs, such as in the Iowa Women’s Study, have been previously shown, but the results were mixed. The two recent consistent findings support the evidence that PUFAs and vegetable fat may reduce the risk of type 2 diabetes. However, the general picture is that intake of SFAs and their associated dietary variables, dietary cholesterol, meat intake, and animal fat are associated with increased risk of diabetes. Only limited evidence is available on a potential detrimental effect of trans fatty acids on glucose metabolism.

The absence of an association between SFA intake and diabetes in both cohorts is rather unexpected. Recently, the results of a large, well-designed, randomized intervention on fatty acids and insulin sensitivity have been published (5). The KANWU Study (5) included 162 healthy volunteers receiving a controlled isoenergetic diet containing either a high proportion of SFA (17.6% of energy) or MUFA (21.2% of energy) for 3 months. Within each group, there was a second random assignment to a supplement of n-3 PUFA from fish oil or a placebo. Introducing the SFA diet reduced insulin sensitivity by 10%, an effect not seen by introducing the MUFA diet (2%). Notably, the detrimental effect of SFA versus MUFA on insulin sensitivity was primarily seen in subjects with a total fat intake below the median value of 37% of energy. The addition of n-3 fatty acids did not influence insulin sensitivity or secretion.

This well-conducted intervention study corroborates the suggestions of a detrimental effect of SFA intake from earlier epidemiological observations (4) and provides evidence for a more beneficial effect of MUFA intake, both of which were not seen in the Iowa Women’s Study (2) or in the Nurses’ Health Study (3). As for MUFA, the low intake of olive oil and the high intake of MUFA from milk products and meat in the cohorts (and thus the high correlation with SFA intake) may be responsible for this. Methodological factors may also play a role. Both studies used the same food-frequency questionnaire, and both studies were performed in a U.S. population, probably with similar sources of fatty acids. In both studies, a weak positive association between SFA and diabetes risk was seen, which disappeared after adjustments for other dietary factors, including MUFA and dietary cholesterol, possibly introducing problems with multicollinearity. Finally, no attempt was made to follow the KANWU suggestion of analyzing modification by total fat intake.

A beneficial effect of n-3 fatty acids was not shown in the Iowa Women’s Study cohort or in the KANWU study. This is in contrast with animal experi-
ments, ecological studies, and three cohort studies (3,4). One of the factors that may explain these contradictory results is that the impact of n-3 PUFAs on insulin sensitivity depends on the ratio of n-6 to n-3 PUFAs in the membranes of the target organs.

Several lines of experimental investigations have now suggested mechanisms through which dietary fatty acids could affect glucose metabolism. Dietary PUFAs (n-6 and n-3) have been shown to reduce triglyceride accumulation in skeletal muscle and possibly in B-cells, factors associated with increased insulin sensitivity (6). PUFAs suppress lipid synthesis in the liver, upregulate fatty acid oxidation in the liver and skeletal muscle, and increase total body glycogen storage. One pathway may be through the fatty acid composition of cell membranes and subsequent changes in hormone signaling. However, fatty acids affect gene expression more directly as they act as natural ligands for genes, such as PPAR and SREBP1.

A noteworthy observation has recently been made by Luan and et al. (7). The PUFA-to-SFA ratio of the diet of non-diabetic subjects was inversely associated with BMI and fasting insulin levels but only in the Ala carriers of the Pro12Ala polymorphism of the PPAR-γ2 gene. These results are not easy to interpret, as the Ala variant is associated with moderately reduced transcription activity and lower BMI and improved insulin sensitivity in some but not all studies. However, this example of gene-diet interaction may also explain the heterogeneity of earlier findings.

Other potential pathways relating PUFA and vegetable fat to diabetes involve differential effects of fatty acids on insulin secretion (4,8) or refer to the role of low-grade inflammation. Proinflammatory cytokines, such as tumor necrosis factor-α, may induce insulin resistance by influencing the function of the insulin receptor (9) and are affected by n-3 PUFA. The current guidelines of the American Hospital Association place increased recognition on the diet as a whole rather than on single nutrients (8). This is a laudable approach from a health education as well as a public health point of view and relates to the prevention of diabetes. Indeed, in the May issue of Diabetes Care, Williams et al. (10) suggested that the adoption of a Western (Anglo) diet may increase the risk of diabetes in Pima Indians. Compared with the Indian diet, the Anglo diet consisted of less complex carbohydrates, dietary fiber, and vegetable protein and presumably less vegetable fat. These results merge the observed relation of various dietary factors (other than PUFAs and vegetable fat) with diabetes incidence (1–5,10).

In summary, observations and interventions published this Spring have now provided evidence confirming earlier suggestions of a significant role of dietary composition in determining the development of type 2 diabetes, independent of obesity. Moderate energy intake (relative to the level of physical activity), increased intake of dietary fiber (soluble as well as nonsoluble), and a reduced intake of saturated fat, partly replaced by starch (1,5) and vegetable fats (PUFA as well as MUFA (2,3,5), are the recommendations that best describe the most recent findings. Importantly, these suggestions are in agreement with recommendations on the prevention of other chronic diseases, such as heart disease (8). The challenge now is not only to elucidate effects of other fatty acids, such as n-3 PUFAs, trans fatty acids, and conjugated linoleic acid, but also to study the role of genetic susceptibility in diabetes prevention and to improve the methods of primary and secondary prevention, all to reduce the burden of diabetes worldwide.

**Editorial**

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**References**


