Lower Prevalence of Impaired Glucose Tolerance and Diabetes Associated With Daily Seal Oil or Salmon Consumption Among Alaska Natives

AMANDA I. ADLER, MD, PHD
EDWARD J. BOYKO, MD, MPH
CYNTHIA D. SCHRAER, MD
NEIL J. MURPHY, MD

OBJECTIVE — To examine the association of seal oil and salmon consumption with impaired glucose tolerance (IGT) and non-insulin-dependent diabetes mellitus (NIDDM) among Alaska Natives.

RESEARCH DESIGN AND METHODS — Screening was performed on 666 Yup'ik Eskimos and Athabaskan Indians ≥40 years old in 15 villages. Self-administered questionnaires were used to obtain partial food frequency data. A case was defined as IGT or NIDDM, either newly discovered or known. Newly discovered cases (11 patients with NIDDM and 17 with IGT) were determined by random blood glucose testing followed by a 2-h 75-g oral glucose tolerance test (OGTT) for those with values ≥6.72 mmol/l or for subjects with unconfirmed histories of glucose intolerance. Known cases included 26 patients with NIDDM and 1 with IGT. Control subjects had random blood glucoses <6.72 or normal OGTT results.

RESULTS — Compared with less-than-daily consumption, both daily seal oil (odds ratio [OR] 0.2, 95% confidence interval [CI] 0.1–0.8) and daily salmon consumption (OR 0.5, CI 0.2–1.1) were associated with a lower prevalence of glucose intolerance, controlling for age, ethnicity, body mass index, and sex. The effects were similar when limited to newly discovered cases: OR 0.3, CI 0.1–1.3 for seal oil and OR 0.4, CI 0.1–1.3 for salmon. Consumption of seal oil at least five times per week was required to reduce risk.

CONCLUSIONS — Consumption of seal oil and salmon, high in ω-3 fatty acids, appears to lower the risk of glucose intolerance and is a potentially modifiable risk factor for NIDDM in Alaska Natives.

From the Department of Epidemiology (A.I.A.) and the Department of Medicine (E.J.B.), University of Washington; the Veterans Affairs Hospital Medical Service (E.J.B.), Seattle, WA; and the Diabetes Program (C.D.S.) and the Department of Obstetrics and Gynecology (N.J.M.), Alaska Area Native Health Service, Anchorage, Alaska.

Address correspondence and reprint requests to Amanda I. Adler, MD, PhD, Fred Hutchinson Cancer Research Center, Public Health Sciences Division, 1124 Columbia St. (MP 381), Seattle, WA 98104.

Received for publication 3 May 1993 and accepted in revised form 13 July 1994.

BMI, body mass index; IGT, impaired glucose tolerance; NIDDM, non-insulin-dependent diabetes mellitus; OGTT, oral glucose tolerance test; OR, odds ratio; CI, confidence interval; PUFA, polyunsaturated fatty acid.

The low prevalence of diabetes in Eskimos has been documented internationally (1). The Alaskan Eskimo age-adjusted prevalence of diagnosed diabetes in 1985 was 0.9% compared with 2.6% for the U.S. population (2,3). Within Alaska and Canada, the prevalence of diabetes in Indians is higher than in Eskimos, but is generally lower than other Indian tribes in which the prevalence may exceed 20% in adults (1,4). This difference in prevalence among populations that share genetic similarities (4), plus the rising prevalence of glucose intolerance in Alaska Native populations (5), suggests the presence of an environmental factor affecting diabetes prevalence.

Alaska Natives traditionally consume a diet high in sea mammals and fish. It is speculated that the low prevalence of diabetes in Eskimos may result from a diet high in ω-3 fatty acids (6). Seal oil ranks fourth among fats, and salmon ranks first among meats and fish most frequently consumed by Alaska Natives (7). We studied the association of these foods with glucose intolerance among the Yup'ik Eskimos and Athabaskan Indians of the Yukon/Kuskokwim Rivers Delta (Fig. 1).

RESEARCH DESIGN AND METHODS

— The study consisted of 556 Eskimos and 110 Athabaskans who were at least 40 years of age from 15 villages, including those studied by Mouratoff (8); participation was voluntary and represented 73% of the villages' population of 914. Self-administered questionnaires, using translators as needed, were used to collect dietary data in the form of partial food frequencies measured as "never" or in times per year, month, or week. The most frequent consumption category was "at least daily." The questionnaire sought information on 25 food items, including traditional (e.g., seal, wild greens) and nontraditional (e.g., beef, candy) foods. A physical activity score was devised based on activities of

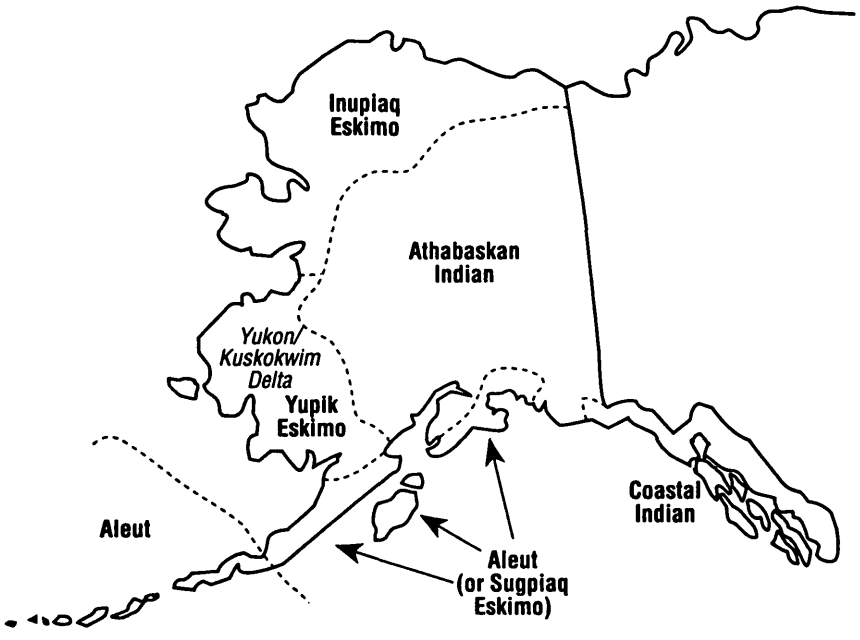

Fig. 1—*Yup'ik Eskimos and Athabaskan Indians of the Yukon/Kuskokwim Rivers Delta.*

traditional life. The food frequency and activity data were not validated. Heights and weights were measured for 93% of subjects using a standard balance beam scale. Body mass index (BMI) was defined as weight (kg)/height (m)^2. "Overweight" was defined using National Center for Health Statistics standards (9).

A case was defined as either newly discovered or known impaired glucose tolerance (IGT) or non-insulin-dependent diabetes mellitus (NIDDM). Known cases were patients who had documentation of NIDDM (10), prescriptions for hypoglycemic medications, or a history of glucose intolerance confirmed in this study by a 2-h 75-g fasting oral glucose tolerance test (OGTT). All other subjects underwent random capillary blood glucose screening (Chemstrip bG and Accu-Chek II, Boehringer Mannheim, Indianapolis, IN). An OGTT was administered to those with a random screening blood glucose of ≥6.72 mmol/l by any one method and interpreted using standard criteria (10). Control subjects were defined by a random blood glucose of <6.72 mmol/l or normal OGTT results.

Patients included 11 newly discovered (1 with a history of IGT) and 26 known cases of NIDDM and 1 known and 17 newly discovered cases of IGT. Forty-six of 55 patients and 203 of 611 control subjects underwent OGTT.

RESULTS— Subject characteristics are shown in Table 1. The average age of the study population was 56.8 (range 40–92), and 54% were women. More Eskimos than Athabaskans ate seal oil (95 vs. 10%), while similar proportions ate salmon (99 vs. 95%). Although there was no association between age and seal oil consumption, daily salmon eaters were more likely to be >70 years old (odds ratio [OR] 1.9, 95% confidence interval [CI] 1.1–3.6) compared with less-than-daily salmon eaters.

Univariate analysis of daily seal oil consumption in association with glucose intolerance suggested a protective effect with an OR of 0.2 (CI 0.1–0.7). In view of their possible association with both seal oil consumption and glucose intolerance, ethnicity, age, BMI, and sex were evaluated as covariates using multivariate logistic regression; confounding was not observed (OR 0.2, CI 0.1–0.8). Controlling for physical activity also did not alter the magnitude of the association (OR 0.3, CI 0.1–1.3). Adjusting for ethnicity, sex, BMI, and age, a slightly diminished protective effect of daily seal oil was observed when limited to patients with NIDDM (OR 0.4, CI 0.1–1.3) or to patients with newly discovered glucose intolerance (OR 0.3, CI 0.1–1.3). Consumption of seal oil at least five times per week was required to reduce risk of glucose intolerance in age-adjusted analyses. Compared with Eskimos who ate seal oil at least five times per week, Eskimos who ate seal oil less than five times per week but at least once per week were significantly more likely to develop glucose intolerance (OR 2.9, 95% CI 1.3–6.4), as were Eskimos who ate seal less than weekly (OR 2.6, 95% CI 1.1–6.1).

Age-, sex-, BMI-, and ethnicity-adjusted analysis of daily salmon consumption also suggested protection against glucose intolerance (OR 0.5, CI 0.2–1.1) when limited to newly discovered patients (OR 0.4, CI 0.1–1.3). Compared with daily salmon consumers, those participants who ate salmon on a less than daily, but more than weekly, basis were twice as likely to have developed glucose intolerance (OR 2.1, 95% CI 1.1–4.1).

None of the 58 people who consumed both seal oil and salmon on a daily basis developed IGT or diabetes compared with 45 of 457 (9.9%) who ate neither seal oil nor salmon on a daily basis.

CONCLUSIONS— The pathophysiological basis of our findings may be the incorporation of dietary fat into the phospholipids of the cellular membrane (11). C20-C22 polyunsaturated fatty acids (PUFAs), and to a lesser extent C20-C22 ω-3 PUFAs (present in arctic sea mammals), in skeletal muscle membranes are associated with lower fasting insulin levels and enhanced insulin sensitivity, which may be a result of changes in insulin receptors, glucose transporters, and/or second messengers (12). Storlein et al. (13) fed rats ω-3 PUFAs and prevented

Table 1—*Characteristics of population by glucose tolerance status*

	Control subjects	IGT	NIDDM
n	611	18	37
Eskimo	517 (84.7)	13 (72.2)	26 (70.3)
Women	321 (52.5)	12 (66.7)	26 (70.3)
Overweight	211 (36.5)	8 (44.4)	19 (51.4)
Age			
40–49	210 (34.4)	4 (22.2)	5 (13.5)
50–59	173 (28.3)	2 (11.1)	6 (16.2)
60–69	131 (21.4)	6 (33.3)	14 (37.8)
≥70	97 (15.9)	6 (33.3)	12 (32.4)
Seal oil intake			
Never	91 (17.3)	5 (29.4)	10 (31.3)
<Monthly	11 (2.1)	0 (0)	0 (0)
≥Monthly but <weekly	84 (15.9)	4 (23.5)	5 (15.6)
≥Weekly but <daily	213 (40.4)	8 (47.1)	14 (43.8)
Daily	128 (24.3)	0 (0)	3 (9.4)
Salmon intake			
Never	8 (1.5)	0 (0)	0 (0)
<Monthly	6 (1.1)	0 (0)	0 (0)
≥Monthly but <weekly	114 (21.6)	2 (12.5)	5 (15.6)
≥Weekly but <daily	270 (51.2)	13 (81.2)	21 (65.6)
Daily	129 (24.5)	1 (6.3)	6 (18.8)

Data are *n* (%). Intake totals reflect food frequency data available on 86% of subjects.

insulin resistance. Bjerve et al. (14) noted significantly lower blood levels of 22:5ω-3 and 22:6ω-3 PUFAs in 325 newly diagnosed NIDDM patients compared with control subjects. Because serum ω-3 PUFAs reflect dietary intake in NIDDM patients (15), one explanation of the data is that dietary ω-3 PUFAs lower the incidence of diabetes. Most studies of ω-3 PUFAs and diabetes have concentrated on glycemic control rather than prevention, and many have shown adverse effects. This may have been because of biases in study design, since adverse effects might occur early and transiently. In one study, 10 g/day of MaxEPA worsened fasting plasma glucose after 3 weeks, but not after 6 weeks (16). While the duration of fish oil trials extend a few months, the dietary patterns among Alaska Natives are lifelong.

In our study, the average daily consumption of ω-3 PUFAs from seal oil was ~8 g. We based this estimate on a 30% ω-3 PUFA content of seal oil (17), its specific gravity (18), and a mean serving of 30 cc (7). Our estimate resembles the seal oil consumption of all Alaska Natives (19) and the ω-3 PUFA intake of 9 g/day by Greenland Eskimos (20) and by Siberian coastal Eskimo and Chukchi (21).

The stronger protective effect of seal oil relative to salmon observed in this study may be due to the higher ω-3 PUFA content of seal oil or to differences between the structure of ω-3 PUFAs of marine mammals and of fish (22). Seal oil may have been eaten more frequently than salmon, since no classification existed for consumption greater than "at least daily." Seal oil contains more ω–9 and ω–11 monounsaturated fatty acids than does salmon (23), which also might account for the difference. Seal oil might also interact with a cofactor correlated with its consumption.

With respect to possible biases, since all subjects did not have OGTTs, patients with NIDDM or IGT may have been misclassified as control subjects. Presuming no dietary differences between individuals correctly and incorrectly designated, misclassification would have caused an underestimation in our findings of a protective effect of diet. Since 160 mg/dl has been recommended as the screening random blood glucose level above which diagnostic testing is recommended (24), our use of a lower, more sensitive level (121 mg/dl) lowers the probability of missed cases. Inclusion of study nonparticipants would likely have strengthened our findings, since Alaska Natives leave their villages for extended periods to hunt and would seem more likely to eat traditionally. The analysis of newly discovered cases discounted the possibility that the presence of glucose intolerance altered nutritional habits in subjects. Yet, the therapeutic use of seal oil by people with undiagnosed symptomatic NIDDM would have caused our findings to underestimate the effect of seal oil.

Because food frequency questionnaires attempt to measure average long-term diet rather than precise short-term diet (25), their use in this study was appropriate. While we did not compare our data to food diaries, self-administered food frequency questionnaires are considered valid, as well as efficient, inexpensive (25,26), and well suited to communities with little dietary diversity (27). Because the data were grouped into large categories, any loss of validity due to misclassification would be minimized.

While diabetes is increasing among Alaska Natives, the proportion of the native diet comprised of fish and sea mammals is decreasing (19). This might be a regrettable occurrence if this diet helps prevent diabetes.

Acknowledgments— Funding was provided by National Institutes of Health Grant DK-44561, Indian Health Service Research Initiative Grant 87–01, and National Cancer Institute Grants 5R35-CA-39779 and 2T32-CA-09168.

References

1. Young TK, Schraer CD, Shubnikoff EV, Szathmary EJE, Nikitin YP: Prevalence of diagnosed diabetes in circumpolar indigenous populations. *Int J Epidemiol* 21: 730–736, 1992
2. Schraer CD, Lanier AP, Boyko EJ, Gohdes D, Murphy NJ: Prevalence of diabetes mellitus in Alaskan Eskimos, Indians, and Aleuts. *Diabetes Care* 11:693–700, 1988
3. Centers for Disease Control: *Diabetes Surveillance*. Bethesda, MD, Department of Health and Human Services, 1991
4. Sievers ML, Fisher JR: Diabetes in North American Indians. In *Diabetes In America*. Harris MI, Hamman RF, Eds. Washington, DC, U.S. Govt. Printing Office, 1985 (DHHS pub. no. NIH 85–1488)
5. Murphy NJ, Schraer CD, Bulkow LR, Boyko EJ, Lanier AP: Diabetes mellitus in Alaskan Yup'ik Eskimos and Athabscan Indians after 25 years. *Diabetes Care* 15: 1390–1392, 1992
6. Lardinois CK: The role of ω-3 fatty acids on insulin secretion and insulin sensitivity. *Med Hypotheses* 24:243–248, 1987
7. Nobmann ED: *Assessment of Current Dietary Intakes of Alaska Native Adults, 1987–1988*. Anchorage, AK, Alaska Area Native Health Service, 1989
8. Mouratoff GJ, Scott EM: Diabetes mellitus in Eskimos after a decade. *JAMA* 226: 1345–1346, 1973
9. National Center for Health Statistics, Najjar MF, Rowland M: Anthropometric reference data and prevalence of overweight, United States, 1976–80. In *Vital Health Statistics*. Series 11, no. 238. Washington, DC, U.S. Govt. Printing Office, 1987 (DHHS publ. no. 87–1688)
10. World Health Organization Study Group: *Diabetes Mellitus*. Geneva, World Health Org., 1985 (Tech. Rep. Ser., no. 727)
11. Field CJ, Ryan EA, Thomson ABR, Clandinin MT: Dietary fat and the diabetic state alter insulin binding and the fatty acyl composition of the adipocyte plasma membrane. *Biochem J* 253:417–424, 1988
12. Borkman M, Storlein LH, Pan DA, Jenkins AB, Chisholm DJ, Campbell LV: The relation between insulin sensitivity and the fatty-acid composition of skeletal-muscle phospholipids. *N Engl J Med* 328:238–244, 1993
13. Storlein LH, Kraegen EW, Chisholm DJ, Ford GL, Bruce DG, Pascoe WL: Fish oil prevents insulin resistance induced by high-fat feeding in rats. *Science* 237:885–888, 1987
14. Bjerve KS, Brekke O-L, Fougner KJ, Midthjell K: Omega–3 and omega–6 fatty acids in serum lipids and their relationship to human disease. In *Dietary Omega-3 and Omega-6 Fatty Acids: Biological Effects and Nutritional Essentiality*. Galli C, Simopoulos AP, Eds. New York, Plenum, 1989, p. 241–251
15. Zambon S, Friday KE, Child MT, Fujimoto WF, Bierman EL, Ensinck JW: Effect of glyburide and omega-3 fatty acid dietary supplements on glucose and lipid metabolism in patients with non-insulin-dependent diabetes mellitus. *Am J Clin Nutr* 56:447–454, 1992
16. Hendra TJ, Britton ME, Roper DR, Waine-Twabe D, Jeremy JY, Dandona P, Haines AP, Yudkin JS: Effects of fish oil supplements in NIDDM subjects. *Diabetes Care* 13:821–829, 1990
17. Ackman RG, Lamothe F: Marine mammals. In *Marine Biogenic Lipids, Fats, and Oils*. Vol. 2. Ackman RG, Ed. Boca Raton, FL, CRC, 1989, p. 179–381
18. Altman PL, Dittmer DS: *Biology Data Book*. 2nd ed. Bethesda, MD, Federation of American Societies for Experimental Biology, 1972
19. Nobmann ED, Byers T, Lanier AP, Hankin JH, Jackson MY: The diet of Alaska Native adults: 1987–1988. *Am J Clin Nutr* 55:1024–1032, 1992
20. Bang HO, Dyerberg J, Sinclair HM: The composition of the Eskimo food in northwestern Greenland. *Am J Clin Nutr* 33: 2657–2661, 1980
21. Nikitin YP, Klochkova E, Mamleeva FR: Comparison of diets in two native Chukotka populations and prevalence of ischemic heart disease risk factors. *Arct Med Res* 50:67–72, 1991
22. Ackman RG: Some possible effects on lipid biochemistry of differences in the distribution on glycerol of long chain n–3 fatty acids in the fats of marine fish and marine mammals. *Atherosclerosis* 70:171–173, 1988
23. Carroll KK, Woodward JH: Nutrition and human health aspects of marine oils and lipids. In *Marine Biogenic Lipids, Fats, and Oils*. Vol. 2. Ackman RG, Ed. Boca Raton, CRC, 1989, p. 435–456
24. American Diabetes Association: Clinical practice recommendations, 1989–1990: screening for diabetes. *Diabetes Care* 13: 7–9, 1990
25. Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, Willett WC: Reproducibility and validity of an expanded self-administered semiquantitiative food frequency questionnaire among male health professionals. *Am J Epidemiol* 135: 1114–1126, 1992
26. Willet WC, Reynolds RD, Cottrell-Hoehner S, Sampson L, Browne ML: Validation of a semi-quantitative food frequency questionnaire: comparison with a 1-year diet record. *J Am Diet Assoc* 87:43–47, 1987
27. Sempos C: Invited commentary: some limitations of semiquantitative food frequency questionnaires. *Am J Epidemiol* 135:1127–1132, 1992