Dietary Fat and Fish Intake and Age-Related Maculopathy

Wayne Smith, BMed, BMath, MPH, PhD, FAFPHM; Paul Mitchell, MD, FRACO, FRCOphth; Stephen R. Leeder, MB, BS, PhD

Objective: To assess whether dietary intake of fat or fish is associated with age-related maculopathy (ARM) prevalence.

Design: Cross-sectional, urban population–based study.

Participants: People (N = 3654) aged 49 years or older.

Main Outcome Measures: Subjects with ARM were identified from masked grading of retinal photographs. A 145-item self-administered, semiquantitative food frequency questionnaire was completed adequately by 88.8% of participants and was used to assess intakes of dietary fat and fish.

Results: A higher frequency of fish consumption was associated with decreased odds of late ARM (odds ratio for frequency of consumption more than once per week compared with less than once per month, 0.5). Subjects with higher energy-adjusted intakes of cholesterol were significantly more likely to have late ARM, with an increased risk for late ARM for the highest compared with the lowest quintile of intake (odds ratio, 2.7).

Conclusion: The amount and type of dietary fat intake may be associated with ARM.

Arch Ophthalmol. 2000;118:401-404

A GE-RELATED maculopathy (ARM) is a leading cause of irreversible blindness in Australia and the United States. The causes of ARM are not known, but there are many hypothesized risk factors. In addition to smoking, a number of cardiovascular diseases and risk factors previously have been found to have statistically significant associations with ARM. These include systemic hypertension, past diagnosis of vascular disease, presence of carotid or lower extremity arterial disease, high serum cholesterol level, body mass index (calculated as the weight in kilograms divided by the square of the height in meters), and plasma fibrinogen level. However, few cardiovascular associations found in individual studies have been reproduced consistently. An association between early ARM and a high intake of saturated fat and cholesterol was reported from the Beaver Dam Eye Study. The relation between diet and atherosclerosis is unproven. However, reasonable evidence suggests that dietary fat intake, particularly dietary intake of saturated fat and cholesterol, is associated with an increased risk for atherosclerosis. It is biologically plausible that higher dietary saturated fat intake promotes atherosclerosis to increase the risk for ARM.

The human retina and macula contain a high proportion of polyunsaturated ω-3 fatty acids, particularly docosahexaenoic acid. Docosahexaenoic acid is found predominantly in oily fish and offal and appears to play an important role in the normal functioning of the retina. Increased consumption of fish and fish oils containing ω-3 fatty acids has been associated with antiatherosclerotic effects in a number of studies, although not all. Few previous studies have examined associations between dietary fat or fish consumption and ARM. In the only study to assess fish consumption, the intake of fish in the population with ARM was relatively low. In the Blue Mountains Eye Study (BMES) population, considerable diversity of fish intake was recorded. Our objective, therefore, is to assess whether dietary intake of fish or fat was associated with ARM.

RESULTS

Characteristics of subjects who consumed relatively little fish are shown in Table 1. Low fish consumption was crudely associated with increasing age, le-
SUBJECTS AND METHODS

The BMES is a population-based survey of vision and common eye diseases in an urban population of 3654 people aged 49 years or older (participation rate, 82.4%). A questionnaire including medical history, smoking history, and family history of late ARM was administered, and subjects underwent a detailed eye examination, including stereoscopic macular photography of at least 1 eye in 3382 participants (98.0%). Details of the survey method and procedures have been described previously.25

The Wisconsin Age-Related Maculopathy Grading System26 was used to grade individual ARM lesions. Age-related maculopathy can be divided into early and late stages. The International ARM Epidemiological Study Group27 described 2 types of late ARM, neovascular and atrophic ARM degeneration. There were 72 cases of late ARM, including 50 neovascular and 22 atrophic cases, identified in the BMES. Early ARM was defined by the presence of soft indistinct or reticular drusen and retinal pigmented abnormalities, in the absence of late ARM in either eye.23 There were 240 early ARM cases identified in the BMES.

Participants also completed a 145-item, semi-quantitative food frequency questionnaire (FFQ) modified from an early FFQ by Willett et al28 for Australian diet and vernacular. The FFQ was attempted and returned by 3267 participants (89.4%), with 2900 (88.8%) usable FFQs, including 46 by participants with late ARM and 182 by participants with early ARM. Characteristics of the FFQ respondents and exclusion criteria have been published previously.29,30 This FFQ was also found to be reliable and to have reasonable concurrent validity compared with weighed food records collected for 1 year in the BMES population.29

Energy-adjusted nutrient intakes from food were calculated using the method described by Willett et al.31 Associations between ARM and categories of nutrient intake for total fat, saturated fat, cholesterol, and monounsaturated and polyunsaturated fats were investigated using logistic regression (SAS [Statistical Analysis System], version 6.12; SAS Institute Inc, Cary, NC) and adjusting for age, sex, current smoking, and family history of late ARM. Tests for trend over quintiles were performed by substituting quintile median values in the adjusted logistic regression models.

male sex, smoking, and a history of angina. More frequent consumption of fish appeared to protect against late ARM, after adjusting for age, sex, and smoking. As shown in Table 2, the protective effect of fish intake commenced at a relatively low frequency of consumption (odds ratio [OR] for intake 1-3 times per month compared with intake <1 time per month, 0.23) and overall had an OR of 0.5. However, there was little evidence of protection against early ARM.

Total and saturated fat intake were associated with a borderline significant increase in risk for early ARM (ORs for highest compared with lowest quintiles of intake, 1.60 and 1.50, respectively), and there was a significant association (P for trend, .05) for increasing prevalence of early ARM with increasing monounsaturated fat intake, as shown in Table 3. Cholesterol intake was associated with a borderline significant increase in risk for late ARM (OR for highest compared with lowest quintiles of intake, 2.71; P for trend, .04).

We found a significant protective association between the frequency of consuming fresh or frozen fish and ARM. Although not significant for all categories of increased consumption, the protection against late ARM due to fish consumption (OR for consumption frequency of more than compared with less than once per month, approximately 0.5) is of the same order of magnitude as the statistically borderline protective effect of higher quintiles of polyunsaturated fat (OR, 0.46). The protective associations between ARM and the frequency of fish consumption and the higher polyunsaturated fat intake have not been reported previously. The Beaver Dam Eye Study reported no associations between ARM and seafood consumption, used as a proxy for ω-3 fatty acid intake,11 and Sanders et al10 found no association using plasma ω-3 fatty acids. However, as noted in the Beaver Dam Eye Study report, consumption of fish in that population may have been too infrequent to identify differences. In contrast, fish intake in our population is likely to be a reasonable marker for dietary ω-3 fatty acid intake, as a considerable proportion of our population report frequent fish consumption (Table 2). Our data suggest the possibility of a threshold protective effect at low levels of fish intake, with no increased protection from ARM at increased fish intake. This is consistent with current interpretation of the published associations between fish intake and cardiovascular disease.24 Consumption of high-fish diets by the elderly has been shown to compromise the status of vitamin E, an important antioxidant needed by the retina22; this could explain the threshold protective effect from dietary fish.

<table>
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Table 1. Subjects With and Without Relevant Cardiovascular Disease Factors Reporting Low Fish Consumption*  

*Low consumption indicates less than 1 serving of fish per month. AMI indicates acute myocardial infarction; CVD, cardiovascular disease. †P < .05.

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The biological plausibility of a protective effect of ω-3 fatty acids against the development of ARM is supported by the high level of polyunsaturated fatty acids in the retina, where they may be active in the maintenance of cell membrane and the constant renewal of retinal components after oxidative damage. Protection against ARM may also be provided by ω-3 fatty acids through a direct or indirect antiatherosclerotic effect.

The relatively large proportion of people with late ARM who did not return usable FFQs (26/72 [36.1%]) provides a potential source of bias. However, there was no significant association between late ARM and return of a usable FFQ, after adjusting for age and sex. It is unlikely that this nondifferential nonresponse has led to a major bias. Antioxidant vitamin intake was not a confounder in any of the associations between ARM and dietary fat and fish intake. A previous report found no significant associations between antioxidant vitamin intake and late or early ARM in this population. Table 1 shows a relatively strong association between decreasing fish intake and increasing age. The logistic regression may have controlled inadequately for age in the adjusted model investigating the association between ARM and lower fish intake, as both are strongly age-related characteristics. This could have resulted in a spurious association, although this is unlikely, as the analysis includes sufficient numbers of subjects without ARM in the older age groups.

For associations between ARM and dietary fat intake, our results are similar to those reported from the Beaver Dam Eye Study. In Beaver Dam, associations were found between the highest compared with the lowest quintile of saturated fat intake and early (OR, 1.8) and late ARM (OR, 1.5). Our equivalent estimates of ORs of 1.50 and 1.61, respectively, agree closely. Similarly, the Beaver Dam Eye Study reported associations between highest compared with lowest quintile of cholesterol intake and early (OR, 1.6) and late ARM (OR, 1.4). These ORs compare reasonably with our estimated ORs of 1.40 and 2.71, respectively. The consistency of the magnitude of these associations across both studies lends credence to the contention that a higher dietary intake of saturated fats and cholesterol may confer an increased risk for ARM.

A survivor cohort effect may explain the failure of many studies to find associations between cardiovascular disease and ARM, if such an association truly exists. Subjects in whom cardiovascular disease develops will often die before late ARM, a relatively rare disease before the age of 70 years, develops. People with severe cardiovascular disease may thus die before they could be included in cross-sectional and case-control studies investigating associations between cardiovascular dis-
eases and ARM. If there is a true association between ath-
erosclerosis and ARM, subjects who survive to develop-
ment of ARM are likely to be protected from the worst
consequences of atherosclerosis, which may remain un-
detectable. However, dietary fat intake differences still
may be detectable among survivors and may be found
to be associated with ARM when atherosclerosis ap-
pears not to be associated.

Despite a likely survivor cohort effect, some studies"12,13 have found increased risk for ARM with a his-
tory of a cardiovascular event or diagnostic signs, but other
studies12,13 have found no associations with vascular
events.

The causal pathway of higher saturated dietary fat
intake, leading to increased atherosclerosis and develop-
ment of ARM, is a plausible explanation for our find-
ing of an association between dietary fat intake and ARM.
Together with the protective association found for ARM
with increasing frequency of fish consumption, our find-
ings suggest that the amount and type of dietary fat in-
take are associated with ARM.

This cross-sectional study, although supported by
findings from the Beaver Dam Eye Study, provides insuf-
icient evidence of dietary fat intake to join tobacco
smoking as an accepted, preventable risk factor for ARM.
Evidence from large, prospective studies is required to
confirm these findings. Identifying preventable risk fac-
tors for ARM, now the most common cause of blindness
in western countries, may be the only way of reducing
the burden of this disease, as current treatments are rarely
effective in the longer term.

Accepted for publication August 26, 1999.

This study was supported by a Research and Develop-
ment Grant Advisory Committee grant from the Australian
Department of Health and Family Services, the Save Sight
Institute, University of Sydney, Sydney, New South Wales,
Australia.

Reprints: Wayne Smith, BMed, BMath, MPH, PhD,
FAPPHM, National Centre for Epidemiology and Popu-
lation Health, Australian National University, Australian Cap-
ital Territory, 0200 Australia (e-mail: wayne.smith@anu.
edu.au).

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