Fish and polyunsaturated fat intake and development of allergic and nonallergic rhinitis

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Background: Rhinitis is one of the most common diseases in childhood. Fish, polyunsaturated fatty acid (PUFA), and vitamin D intakes have been hypothesized to affect the risk of allergic disease; however, it is unclear whether these are linked to the development of rhinitis.

Objective: We sought to assess potential associations between consumption of fish, dietary n-3 and n-6 PUFAs, and vitamin D at age 8 years and development of allergic rhinitis (AR) and nonallergic rhinitis (NAR) between the ages of 8 and 16 years.

Methods: We included 1970 participants from a birth cohort. Data on dietary intake was obtained from a food frequency questionnaire at age 8 years. The rhinitis definition was based on questionnaires and IgE measures.

Results: The prevalence of rhinitis symptoms at age 8 years was 19% (n = 380). Among the 1590 children without rhinitis symptoms at age 8 years, 21% (n = 337) had AR between ages 8 and 16 years, and 15% (n = 236) had NAR. Regular intake of oily fish and higher long-chain n-3 PUFA intake were associated with a reduced risk of cumulative incidence of NAR (adjusted odds ratio, 0.52 [95% CI, 0.32-0.87] for oily fish; odds ratio, 0.45 [95% CI, 0.30-0.67] for highest vs lowest tertile of long-chain n-3 PUFAs; *P* trend < .001). The results for rhinitis, irrespective of AR and NAR, were in line with the findings for NAR.

Conclusion: Regular consumption of oily fish and dietary long-chain n-3 PUFAs in childhood might decrease the risk of rhinitis, especially NAR, between the ages of 8 and 16 years. (J Allergy Clin Immunol 2015;136:1247-53.)

Key words: *Adolescent, allergic rhinitis, BAMSE, children, diet, fatty acid, fish, nonallergic rhinitis, prospective studies, vitamin D*

Rhinitis is one of the most common chronic diseases in childhood.[1,2] Noninfectious rhinitis can be distinguished into allergic rhinitis (AR) and nonallergic rhinitis (NAR).[3,4] In adolescent populations with rhinitis, about 1 in 4 seem to have NAR.[5] A known risk factor for both AR and NAR is parental allergic disease.[6-8] However, few modifiable risk factors have been identified, especially for NAR.[6]

Changes in dietary habits during the past decades, including fish consumption, have been suggested to play a role in the increase of allergic diseases, including rhinitis.[9,10] Oily fish is rich in long-chain n-3 polyunsaturated fatty acids (PUFAs) and vitamin D, which have been suggested to decrease the risk of allergic disease through their immunomodulatory properties,[11,12] whereas n-6 PUFAs and an increased n-6/n-3 ratio have been suggested to increase the risk.[11]

In some studies, including our birth cohort, regular intake of fish in infancy has been associated with a reduced risk of rhinitis at preschool age[13-16] and up to age 12 years.[17] The incidence of rhinitis is high at school age and during adolescence,[2,18] and therefore it is of interest to examine whether school-age consumption of fish, dietary PUFAs, and vitamin D can affect the risk of rhinitis. Previous studies on fish and PUFA intake in school age have assessed intake at the same time as the outcome, and in these studies fish consumption has not been associated with rhinitis,[19-23] whereas studies on PUFA intake and rhinitis have been inconclusive.[24,25] Although few studies have examined the association between vitamin D status and rhinitis in children, an inverse association between vitamin D status at age 6 years and rhinoconjunctivitis at age 14 years was recently observed in a prospective cohort.[26] In previous studies of the relation between fish, PUFA, and vitamin D consumption and rhinitis in childhood, IgE reactivity to common allergens has rarely been included in the definition of rhinitis, which reduces the possibility of exploring associations for AR and NAR separately.

In our birth cohort with longitudinal data, we examined potential associations between fish intake, including types of fish, dietary n-3 and n-6 PUFAs, and vitamin D, at age 8 years and cumulative incidence of AR and NAR between ages 8 and 16 years.

METHODS

Study design and study population

This study is based on a population-based birth cohort, the Children, Allergy, Milieu, Stockholm, an Epidemiological study (BAMSE), to which 4089 newborns were recruited between February 1994 and November 1996 in Stockholm, Sweden. Baseline information was obtained through a parental questionnaire shortly after birth, and follow-ups have taken place throughout

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Supported by the Stockholm County Council; the Swedish Research Council; the Swedish Research Council Formas; the Swedish Heart-Lung Foundation; the Swedish Asthma and Allergy Association; the Swedish Research Council for Health, Working Life and Welfare; and the European Commission's Seventh Framework 29 Program MeDALL (grant agreement no. 261357). Thermo Fisher Scientific kindly provided the reagents. The funding sources had no active role in the conducted research.

Disclosure of potential conflict of interest: J. Magnusson and A. Bergström have received research support from the Swedish Research Council Formas and the Swedish Research Council. M. Westman has received payment for manuscript preparation from MEDA. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication October 29, 2014; revised May 6, 2015; accepted for publication May 14, 2015.

Available online July 4, 2015.

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0091-6749

http://dx.doi.org/10.1016/j.jaci.2015.05.030

Abbreviations used
AA: Arachidonic acid
ALA: α-Linolenic acid
AR: Allergic rhinitis
BAMSE: Children Allergy, Milieu, Stockholm, an Epidemiological study
FFQ: Food frequency questionnaire
LA: Linoleic acid
NAR: Nonallergic rhinitis
OR: Odds ratio
PUFA: Polyunsaturated fatty acid

childhood.[27,28] The most recent follow-up took place at age 16 years; adolescents answered a questionnaire, and the response rate compared with the baseline cohort was 76%.

At 8 and 16 years of age, participants who answered the respective questionnaire were invited to a clinical examination. At the 8-year examination, the child's diet was assessed by using a food frequency questionnaire (FFQ; n = 2614). At both ages 8 (n = 2470 [60%]) and 16 (n = 2547 [62%]) years, participants provided blood samples, which were analyzed for IgE antibodies with ImmunoCAP to common inhalant allergens by using the Phadiatop mix (birch, timothy, and mugwort pollen; cat, dog, and horse dander; and *Cladosporium herbarum* and *Dermatophagoides pteronyssinus*; Thermo Fisher Scientific, Uppsala, Sweden). Blood samples that scored positive for the Phadiatop mix were analyzed for allergen-specific IgE antibodies to the single allergens mentioned above. A technical cutoff was set at an IgE level of 0.35 kU/L or greater, according to the manufacturer's instructions.

Participants with baseline questionnaire data, data on nutrient and total fish intake at age 8 years, and outcome data at age 16 years were included in the present study (n = 1970, 48% of original cohort). Inclusion in the study is described in detail in Fig 1. All parts of BAMSE have been approved by the Ethics Committee of Karolinska Institutet, Stockholm, Sweden, and informed consent from the study participants has been obtained.

Dietary assessment

Diet at age 8 years was assessed by using an FFQ with 98 foods and beverages frequently consumed in Sweden. The participants were asked to indicate how often on average they had consumed these in the previous 12 months, and 10 response categories were predefined (never, <1 time per month, 1-3 times per month, 1 time per week, 2 times per week, 3-4 times per week, 5-6 times per week, 1 time per day, 2 times per day, and ≥3 times per day). Most often the FFQ was filled out by a parent (57%) or a parent together with the child (40%). With regard to fish consumption, participants were asked about intake of herring/mackerel and salmon fishes (categorized as oily fish), as well as codfish/pollock/pike, fish fingers, and tuna fish. Intakes of dietary PUFA and vitamin D were computed from the FFQ by multiplying the frequency of consumption of each food item by its nutrient content per serving and summarized over food and beverages by using composition values obtained from the Swedish Food Administration Database.[29] Nutrient intakes were adjusted for total energy intake by using the residuals method.[30] PUFAs assessed were linoleic acid (LA; 18:2n-6), α-linolenic acid (ALA; 18:3n-3), arachidonic acid (AA; 20:4n-6), eicosapentaenoic acid (20:5n-3), docosapentaenoic acid (22:5n-3), and docosahexaeonic acid (22:6n-3).

Definition of outcomes

Rhinitis symptoms at age 8 years. These symptoms included parent-reported sneezing or runny or blocked nose without common cold or flu in the last 12 months and/or nose or eye symptoms in contact with furred pets and/or pollens after 4 years of age.[3]

AR at age 16 years. AR included adolescent-reported sneezing or runny or blocked nose without common cold or flu or in contact with furred pets, pollens, and/or mites in the last 12 months in combination with sensitization to any of the inhalant allergens tested (Phadiatop ≥0.35 kU/L).[3]

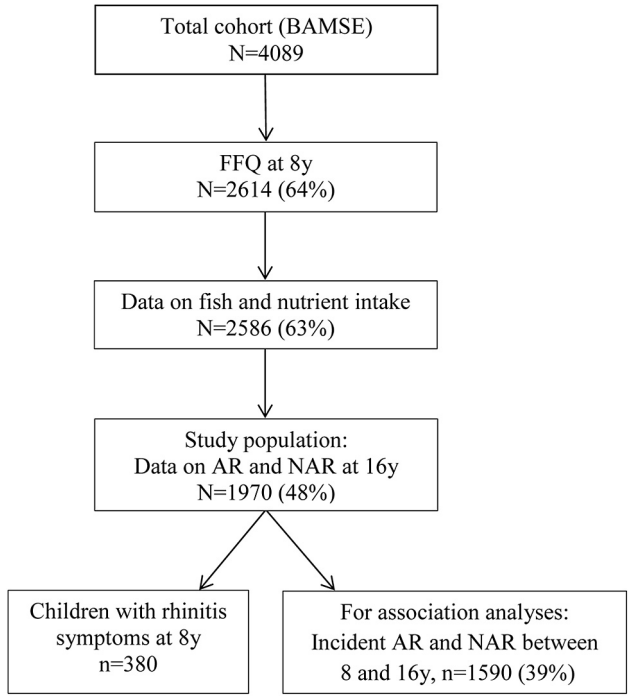

FIG 1. Flow chart of inclusion into the study population and analyses of the cumulative incidence of AR and NAR between ages 8 and 16 years.

NAR at age 16 years. NAR included adolescent-reported symptoms as above with no sensitization (Phadiatop <0.35 kU/L).[3]

Statistical analyses

The distribution of selected background characteristics for the study population and for the total cohort was compared with a 1-sample *t* test. Fish intake was divided into dichotomous variables less than 2 times a week or 2 or more times a week for total fish and less than 1 time a week or 1 or more times a week for oily fish, cod/pollock/pike, and fish fingers. PUFA and vitamin D intakes were divided into tertiles. PUFAs were analyzed as single fatty acids (ALA, LA, and AA) and grouped together to total PUFA, n-6 (LA and AA), and long-chain n-3 (docosahexaeonic acid, eicosapentaeonic acid, and docosapentaenoic acid) PUFAs. We also analyzed the n-6/n-3 ratio. The outcome was analyzed as the cumulative incidence of AR and NAR between ages 8 and 16 years by excluding children with rhinitis symptoms at age 8 years (n = 380, Fig 1), and the reference category consisted of adolescents with no rhinitis symptoms and no sensitization to inhalant allergens at age 16 years. Analyses of associations between exposure and outcome were done with multinomial logistic regression. The results are presented as adjusted odds ratios (ORs) with 95% CIs. Tests for trends in analyses of PUFA and vitamin D intake were performed, assigning the median value of each tertile to all subjects in that tertile, which then was used as a continuous variable in the model.

Traditional potential confounding factors for which we tested were sex, allergic heredity, maternal age, maternal smoking during pregnancy or the child's first months, older siblings and socioeconomic status (baseline questionnaire), breast-feeding duration and fish consumption in infancy (1-year questionnaire), and parental origin, indoor moist, furred pet ownership, parental smoking, socioeconomic status, energy intake, supplement use, and overweight status (8-year questionnaire). In the first step analyses were unadjusted because no factor changed crude ORs by 5% or greater. In a second step food groups (total intake of dairy products, meat, cereals, fruits, and vegetables) were tested as potential confounding factors in analyses of fish intake. No food group changed crude ORs by 5% or greater, and fish analyses were only adjusted for the other types of fish. In addition, in analyses of PUFAs and vitamin D, nutrients were tested as possible