of onset of allergic disease remains a complicated amalgam of genetic and environmental contributions that have yet to be fully understood.

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Is There a March From Early Food Sensitization to Later Childhood Allergic Airway Disease? Results From Two Prospective Birth Cohort Studies

Alduraywish SA, Standl M, Lodge CJ, et al. *Pediatr Allergy Immunol*. 2017;28(1):30–37

PURPOSE OF THE STUDY. To investigate the association between food sensitization in the first 2 years of life and subsequent asthma and allergic rhinitis (AR) by age 10 to 12 years.

STUDY POPULATION. The study consisted of 2 independent cohorts, with 620 subjects from the high-risk (first-degree relative with atopy) Melbourne Atopic Cohort Study (MACS) and 3094 subjects from the German population-based birth cohort study called LISAplus. Both studies were conducted in countries with relatively high income and high rates of food sensitization and allergic diseases.

METHODS. For both cohorts, researchers assessed sensitization to common aeroallergens and food allergens, with researchers in the MACS doing so at 6, 12, and 24 months via skin prick tests (wheal size ≥2 mm) and researchers in the LISAplus doing so at 2 years of age via serum-specific immunoglobulin E antibody level (≥0.35 kU_A/l). Allergic outcomes were defined by questionnaire responses at 10 (LISAplus) and 12 (MACS) years. Logistic regression analysis was performed to calculate odds ratios that were adjusted (aORs) for confounding factors (eczema and/or wheeze by the age at which sensitization was assessed).

RESULTS. Sensitization to food only, compared with non-sensitized children, at 12 months in the MACS and 24 months in the LISAplus was associated with an increased risk of current asthma (aOR = 2.2 in the MACS; aOR = 4.9 in the LISAplus), with similar results for AR. Cosensitization to food and aeroallergens was a stronger predictor of asthma and AR at any tested point in both cohorts (at 24 months: asthma aOR = 8.3 in the MACS and aOR = 14.4 in the LISAplus; AR aOR = 3.9 in the MACS and aOR = 7.6 in the LISAplus).

CONCLUSIONS. The findings of these prospective birth cohort studies suggest that food sensitization in the first 2 years of life leads to an increased risk of the subsequent development of asthma and AR.

REVIEWER COMMENTS. The role of food sensitization in the atopic march from eczema to allergic airway disease is not fully clear. The authors of this study establish a link between early food sensitization and asthma and AR at age 10 to 12 years, even while controlling for confounding factors such as aeroallergen sensitization and early-life eczema and/or wheeze. This association is increasingly relevant in light of recent evidence that early peanut introduction can successfully prevent peanut allergy. With this study, the authors raise the as-of-yet unanswered question of whether such interventions could potentially impact not only the incidence of food allergy but also the subsequent development of allergic rhinitis and asthma.

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Fish Intake During Pregnancy or Infancy and Allergic Outcomes in Children: A Systematic Review and Meta-analysis

Zhang GQ, Liu B, Li J, et al. *Pediatr Allergy Immunol*. 2017;28(2):152–161

PURPOSE OF THE STUDY. To review the effect of fish intake during pregnancy or infancy on allergic outcomes.

STUDY POPULATION. This was a meta-analysis of 1 randomized controlled trial (RCT) and 13 prospective cohort studies. The researchers conducting the RCT enrolled infants at risk for atopy (at least 1 first-degree relative affected by atopy, asthma, or allergy by self-report). The researchers conducting the cohort studies enrolled healthy pregnant women or infants without selection for atopic disease. Studies were conducted in North America, Europe, and Asia.

METHODS. PubMed, Embase, and the Cochrane Central Register of Controlled Trials were searched for records reporting the effect of dietary fish intake during pregnancy or infancy on clinical outcomes of allergic disease or sensitization in children. In all studies, the primary intervention was high versus low or no fish intake during pregnancy or infancy. Outcomes of interest were atopic dermatitis (AD), allergic rhinitis (AR), wheezing, asthma, and food allergy defined by parental report of symptoms or physician diagnosis (direct or by parental report), and sensitization (positive skin prick test result or elevated specific immunoglobulin E) to any food or inhalant allergen. Statistical analysis was performed with attempts to control for confounding factors, family history of allergic disease, and early signs of atopy.

RESULTS. In 1 RCT, researchers enrolled 123 mother-child pairs to receive 300 g of farmed salmon per week or a habitual diet low in oily fish starting at 20 weeks' gestation. Eighty-six infants were evaluated at 6 months,

with no significant differences in immunoglobulin E, AD, wheeze, or sensitization to food or aeroallergens. The cohort studies of maternal fish intake also found no effect on odds ratios for rates of sensitization, AD, AR, wheeze, or asthma. High fish intake during infancy was associated with a 39% reduction in eczema and a 46% reduction in AR. A borderline association with sensitization was found at 4 years of age but was lost by 8 years. No effect was found on wheeze or asthma. There was no study in which researchers reported an association between fish intake during pregnancy or infancy with food allergy.

CONCLUSIONS. Fish intake during infancy is associated with a lower risk of AR and eczema, whereas maternal intake of fish during pregnancy is not.

REVIEWER COMMENTS. Oily fish are a rich source of n-3 long-chain polyunsaturated fatty acids such as docosahexaenoic acid and eicosapentaenoic acid, which have been suggested to lower the risk of allergic disease through anti-inflammatory effects. The mechanism underlying the association between fish intake in infancy and lower risk of AR and AD remains unclear. Furthermore, the findings of this meta-analysis are potentially limited by publication bias and reverse causation (avoidance of fish because of early signs of atopy). Current expert recommendations are to introduce solid foods beginning at 4 to 6 months of age without delaying the introduction of highly allergenic foods, such as fish.

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Prenatal Fish Oil Supplementation and Allergy: 6-Year Follow-up of a Randomized Controlled Trial

Best KP, Sullivan T, Palmer D, et al. *Pediatrics*. 2016; 137(6):e20154443

PURPOSE OF THE STUDY. To assess whether prenatal supplementation with ω-3 (n-3) long-chain polyunsaturated fatty acids (LCPUFA) exerts a protective effect on the development of immunoglobulin E–mediated allergic conditions at 6 years of age in a prospective birth cohort.

STUDY POPULATION. A total of 706 children with a family history of allergic disease were enrolled into this study as part of the Docosahexaenoic Acid to Optimize Mother Infant Outcome trial.

METHODS. Women with a singleton pregnancy (<21 weeks' gestation) were recruited from the Docosahexaenoic Acid to Optimize Mother Infant Outcome randomized controlled trial (RCT) during an antenatal clinic visit. Participants were randomly assigned in a double-blind manner to receive either 500 mg of fish oil concentrate (~800 mg/day docosahexaenoic acid and 100 mg/day eicosapentaenoic acid) or 500 mg of vegetable oil from 21 weeks' gestation until delivery. Women were eligible to enroll in the follow-up study if their unborn children had a family history of atopic disease. Eligible offspring were evaluated in person at age 6 years for allergic disease via a validated questionnaire (International Study of Asthma and Allergies in Childhood), which assessed symptoms experienced over the previous 12 months and included skin prick testing for common food and environmental aeroallergens.

RESULTS. A total of 668 participants from the initial cohort were eligible for the follow-up study. Participant demographics were similar between the 2 groups. Seventy percent of participants had a history of maternal allergic disease compared with 54% who had a history of paternal allergic disease; 24% had a history of atopic disease in both parents. There were no significant differences in the reporting of allergic disease (eczema, wheeze, or rhinitis) on a symptom-based questionnaire between the n-3 LCPUFA and control groups. Rhinitis was the most common symptom (31.5%) affecting the birth cohort. There was also no difference between the groups in percent sensitized to at least 1 allergen on skin prick testing. The only minor difference was a reduction in the percentage sensitized to 1 of the common house dust mite allergens, *Dermatophagoides farinae* (13.4% vs 20.3%; adjusted relative risk, 0.67; 95% confidence interval, 0.44–1.00; $P = .0495$), in the intervention group.

CONCLUSIONS. Prenatal supplementation with n-3 LCPUFA did not reduce the development of allergic disease or sensitization in participants with a family history of atopy compared with control participants at the 6-year follow-up evaluation.

REVIEWER COMMENTS. The quest to find a prenatal intervention that effectively prevents the development of allergic conditions in children continues. To date, this study is the largest RCT in which the researchers assessed the prenatal effect of fish oil supplementation. One of the strengths of the study includes its large sample size and high retention rate. However, no significant differences in primary clinical outcomes of eczema, wheeze, or rhinitis were detected, which is in contrast to previous RCTs, which vary in methodology and age at follow-up. Challenges from similar prenatal interventional studies arise from determining the type of intervention (n-3 fatty acids, vitamin D, probiotics, and prebiotics), the timing and duration of intervention, and what type of product and dosing to use. Although prenatal interventions such as these generally offer little risk to mother or infant, further studies are warranted

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