

REGULAR ARTICLE

Early fish introduction is associated with less eczema, but not sensitization, in infants

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ABSTRACT

Objective: To investigate if the development of allergic diseases during the child's first 18 months of life is influenced by the time at which different food items were introduced into the child's diet.

Method: A birth cohort of 184 children was followed to 18 months of age. Diaries were used to document feeding practices, and parental interviews were performed at 6 and 12 months of age, probing for symptoms suggesting allergic disease, general health-related issues and food introduction regimes. Symptoms promoted prompt clinical examination, and all children were examined clinically, and tested for sensitization to common airborne and food allergens at 18 months of age.

Results: The earlier the fish was introduced into the child's diet the lower was the frequency of eczema. This association remained after control for confounding factors. The timing of fish introduction and asthma development showed a similar pattern, but did not reach statistical significance. Sensitization was not influenced by the timing of fish introduction. Other food items or feeding practices did not seem to influence allergy development.

Conclusion: Early introduction of fish into the child's diet was associated with less eczema development, and a tendency to less asthma. Sensitization was not associated with the timing of fish introduction.

INTRODUCTION

Allergic diseases are common chronic conditions in children, and so far primary prevention strategies have not been very successful. Prolonged breastfeeding and diet regimes to lactating mothers and infants have in this context been advocated, but these measures have so far not been effective in preventing allergy (1). These prevention strategies were based on the notion that late introduction, or a general avoidance, of potential allergens would less likely result in sensitization and allergy development. However, healthy persons are not ignorant to allergens; they have developed immunological tolerance (2).

More recently, food stuffs and feeding practices that promote tolerance and protect against allergy have come into focus. This includes both specific food items *per se*, but also social or cultural changes in feeding practices that may affect a child's risk to develop allergy. Such changes have been observed in children of Asian origin, living in the UK. A switch from a more traditional Asian menu, to a British diet, parallels an increased risk of atopy and bronchial hyper-responsiveness (3). A similar phenomenon has been seen in former East Germany after the unification; with increasing prevalence of allergies paralleling a switch from butter to margarine consumption (4–6). Furthermore, in rural Crete, adherence to a traditional Mediterranean diet

during childhood, rich in fruit, vegetables and nuts, are associated with a low prevalence of asthma and allergic rhinitis (7). Also, early introduction of peanuts into the child's diet seems to reduce the prevalence of peanut allergy in school-aged children (8).

Early consumption of fish has also been associated with a lower prevalence of allergy in some recent studies. In a Norwegian birth-cohort study, a reduced frequency of allergic rhinitis at 4 years of age was seen in children given fish during the first year of life (9). Similar findings have been reported by others. Kull et al. (10) report less sensitization and allergic disease at 4 years of age in children given fish before the age of 1 year. Alm et al. (11) report less eczema in 1-year old children, given fish before the age of 9 months. However, alternative explanations to such an association are selection bias and reverse causation, i.e. that fish is introduced later in children prone to develop allergy, because of allergy in parents or elder siblings, or that fish is postponed in children who themselves have developed food allergy or eczema. The beneficial effect of early fish introduction therefore merits further study in more detail.

Here, we have investigated the relation between time at introduction of various food items and risk of allergy development in the ALLERGYFLORA birth cohort (12). The aim of ALLERGYFLORA is to prospectively investigate

allergy development in relation to factors in early life that may protect or enhance the risk for such diseases with focus on the intestinal microbiota. Parents were approached already at the maternity centre, before the child was born and a close follow-up schedule was employed during the first year of life. Registration of the child's diet by the parents was also part of the study protocol, and the aim of this study was to analyse whether the feeding patterns influence the risk of allergy development. Especially, the timing of introducing different food stuffs in relation to sensitization and development of clinical allergy was focused.

MATERIAL AND METHODS

Subjects

The ALLERGYFLORA birth-cohort study started in 1998. Between 1998 and 2003, 206 pregnant mothers were approached at maternal clinics in Mölndal, a community in the Gothenburg area, Sweden. To achieve a high proportion of children with allergic symptoms and to maximize compliance with a demanding study protocol, we mainly targeted families with at least one parent with a history of allergic disease. A smaller group of healthy parents was included in a proportion of 5:1. Inclusion was carried out on day 1–3 after delivery, if the child was born at term (≥ 38 weeks gestational age) at Sahlgrenska University Hospital/Mölndal, and did not receive mechanical ventilation. Nineteen children could not be recruited; one was stillborn, one mother had post partum psychosis, one family had moved from the area before the child was born. Sixteen children were either born on a holiday lasting for more than 3 days, or midwives at the delivery ward were not able to contact the study nurse in time. Thus, during the 5-year recruitment period, 187 children entered the study, 184 of whom were followed up to 18 months of age. Two families changed their minds during the follow-up period, decided not to participate. The third drop out was because of maternal illness.

The study was approved by the Ethic Committee of the Sahlgrenska Academy, University of Gothenburg, Sweden.

Follow-up and recording of feeding pattern

A structured interview was conducted by the study nurse on recruitment (day 1–3), focusing on the pregnancy and the delivery, the family and housing standards. A diary was given to the parents, and they were asked to note major events such as duration of breastfeeding, food introduction and diseases of the infant during the child's first 6 months of life. A second diary was used for the 6–12-month period. Data from these diaries were recalled during structured telephone interviews by the study nurse when the child was 6 and 12 months old. The study nurse had also regular contact with the parents at week 1, 2, 4 and 8, when stool samples for bacterial cultures were collected (not reported in this study).

Clinical and laboratory examination for allergy diagnoses

At 18 months of age, the child was examined by a paediatric allergist. The examination included a medical chart review,

a structured interview covering health issues in the first 18 months and current family aspects. A physical examination was performed, and venous blood collected for laboratory tests. The child was also seen in between follow-ups by study paediatricians (allergist or gastroenterologist) if he/she developed symptoms suggestive of allergic disease.

Laboratory tests

At 18 months, blood samples were analysed for total eosinophil counts, total IgE, 6-mix food tests and Phadiatop® (Phadia/Pharmacia Diagnostics, Uppsala, Sweden). If positive, the sample was further analysed for specific IgE against timothy, mugwort, dog, cat, horse, house dust mite, *Cladosporium*, cow's milk, hen's egg, fish, wheat, soy and peanut (Immunocap®; Phadia/Pharmacia Diagnostics). An allergen specific IgE-level of ≥ 0.35 kU/L was considered positive.

In the evaluation of children referred to the study paediatrician before 18 months of age because of symptoms, allergen-specific IgE-tests (Immunocap®; Phadia/Pharmacia Diagnostics) were used, or skin prick tests performed in accordance with European guidelines (13). We used histamine 10 mg/mL as positive control, and allergen diluents as negative control. Standard extracts were used for specific allergens (Soluprick SQ; ALK-Abello AS, Hørsholm, Denmark). A weal diameter ≥ 3 mm was considered positive.

Diagnostic groups

Based on clinical examination and laboratory tests, the following diagnostic groups were defined:

Eczema: Eczema ever in the first 18 months. Diagnosed by study paediatrician, and full-filling Williams' criteria (14).

Asthma: At least three episodes of wheeze in the first 18 months of life, in combination with other manifestations of allergy (eczema, rhinoconjunctivitis or food allergy), or with wheeze/breathing problems in between colds, or chronic wheeze lasting for at least 4 weeks. Diagnosis was made by study paediatrician at 18 months, based on information from medical case notes, interview and physical examination.

Food allergy: Food allergy ever, diagnosed by study paediatrician at 18 month of age, summarizing diagnostic evaluations in the first 18 months. A positive diagnosis was based on symptoms (an immediate- or late-onset reaction after ingestion of the specific food, followed by a clear and prompt clinical improvement when eliminating the food allergen), supported by: open food challenge tests, and/or a positive specific allergy test (specific IgE ≥ 0.35 KU/L or skin prick test ≥ 3 mm), and/or eosinophilic inflammation in mucosal gastro-intestinal biopsies, and/or multi-organ reactions.

Sensitization: A positive Phadiatop® or 6-mix food test at 18 months of age.

Variables used to control for reversed causation and selection bias

Eczema 6 months: Eczema ever in the first 6 months. Parental report from telephone interview at 6 months.

Wheeze 6 months: Wheeze ever in the first 6 months. Parental report from telephone interview at 6 months.

Adverse reaction to cow's milk in the first 6 months of life: Parental report from telephone interview at 6 months.

Parental history of allergy: A doctor's diagnosis of asthma, rhinoconjunctivitis or eczema.

Statistics

Statistical analyses were performed with SPSS 15.0.1.1 (SPSS Inc., Chicago, IL, USA). The Monte Carlo Exact Test method was used to compare proportions, and for trend analysis. The Spearman's rho was used for bivariate correlations, and the non-parametric Mann-Whitney test and Median tests for differences between continuous data. Binary logistic regression with the 'Forced Entry method' was used to adjust for confounding variables, and the curve fitness controlled by Hosmer and Lemeshow Test. Eczema was used as the dependent variable. Independent variables were age when fish was introduced, ongoing breastfeeding at 6 months of age, as well as maternal and paternal history of allergy. The significance level was set to 0.05.

RESULTS

Demographic data for the 184 children in the study cohort are shown in Table 1. Twenty-five per cent of the children developed eczema, 5% asthma and 8% food allergy in the first 18 months. Fifteen per cent were sensitized by 18 months of age as shown by a positive 6-food mix (15%) and Phadiatop (2%). Of the 14 children who developed food allergy, nine children had symptoms elicited by cow's milk only, three by cow's milk and hen's egg, one by hen's egg only and one by cow's milk, hen's egg, soy and peas. No child developed sensitization or clinical allergy to fish or wheat during the observation period.

Data on the time of introduction of different food items during the child's first 18 months, and duration of exclusive and partial breastfeeding, are presented in Table 2. The majority of the children (88%) were breastfed, and 76% of

Table 2 Age when different food items were introduced during the child's first 12 months of life

	Number (%)	Age in months Median (25th, 75th)
Breastfeeding		
Any period	163 (88)	
At 6 months	139 (76)	
At 12 months	19 (10)	
Exclusive breastfeeding – duration		4 (3.5, 4.5)
Partial breastfeeding – duration		7.5 (4.5, 9.0)
Cow's milk-based products*		5 (4.0, 6.0)
Fruit		5 (4.0, 5.0)
Solids†		4 (4.0, 5.0)
Fish		10 (6.0, >12)
Hen's egg		11.8 (9.0, >12)

Ages are given in median months. 25th and 75th percentiles are given within brackets.

*All types of cow's milk-based products including infant formula.

†Potatoes, root vegetables, vegetables and meat.

the children still received some breast milk at 6 months of age. The median duration was 4 months for exclusive and 7.5 months for partial breastfeeding. Formulas and other cow's milk-based products were introduced at a median age of 5 months. Solids, such as potatoes, root vegetables, vegetables and meat, were introduced at a median age of 4 months, fruit at 5 months, fish at 10 months and hen's egg close to 12 months.

We analysed if the feeding pattern differed between children who developed eczema, asthma or food allergy, when compared to healthy children, or between sensitized and non-sensitized children (Table 3).

Fish was introduced at a later age in eczematous and food allergic children, when compared to healthy children. A similar pattern was seen for hen's egg. A statistically significant trend was seen between fish introduction and eczema development, i.e. earlier introduction of fish was associated with a gradually lower frequency of eczema (Fig. 1A). Even though hen's egg tended to be introduced at an older age in children with eczema, no significant trend between age of introduction and the frequency of eczema was seen (Fig. 1B).

To evaluate if late introduction of fish and hen's egg was a cause or a consequence of the disease, we analysed the effect of possible confounding factors on timing of introduction of different food items (Table 4). A later introduction of both fish and hen's egg was seen if the mother had a history of allergy, as well as if the child had had adverse reactions to cow's milk in the first 6 months of life. But introduction of fish and egg was unrelated to eczema or wheeze in the child's first 6 months of life. To eliminate one of the factors causing selection bias, we excluded the 14 children who showed adverse reactions to cow's milk during the first 6 months of life. Despite elimination of this significant confounder, children with eczema had fish introduced at older age ($p = 0.031$, Median test). A possible association between hen's egg and eczema was tested in the same way,

Table 1 Demographic data

	Number	%
Total number of children	184	
Boys	93	50
Maternal history of doctor-diagnosed asthma, ARC* or eczema	91	49
Paternal history of doctor-diagnosed asthma, ARC* or eczema	75	41
Any parent with a history of doctor-diagnosed asthma, ARC* or eczema	148	80
Asthma	10	5.4
Eczema	46	25
Food allergy	14	7.6
Sensitization	25	15†

*Allergic rhinoconjunctivitis.

†Percentage figure based on 169 children.

Table 3 Duration of breastfeeding, and age in months when different food items were introduced, in relation to a diagnosis of 'allergic' disease, or to sensitization at 18 months of age

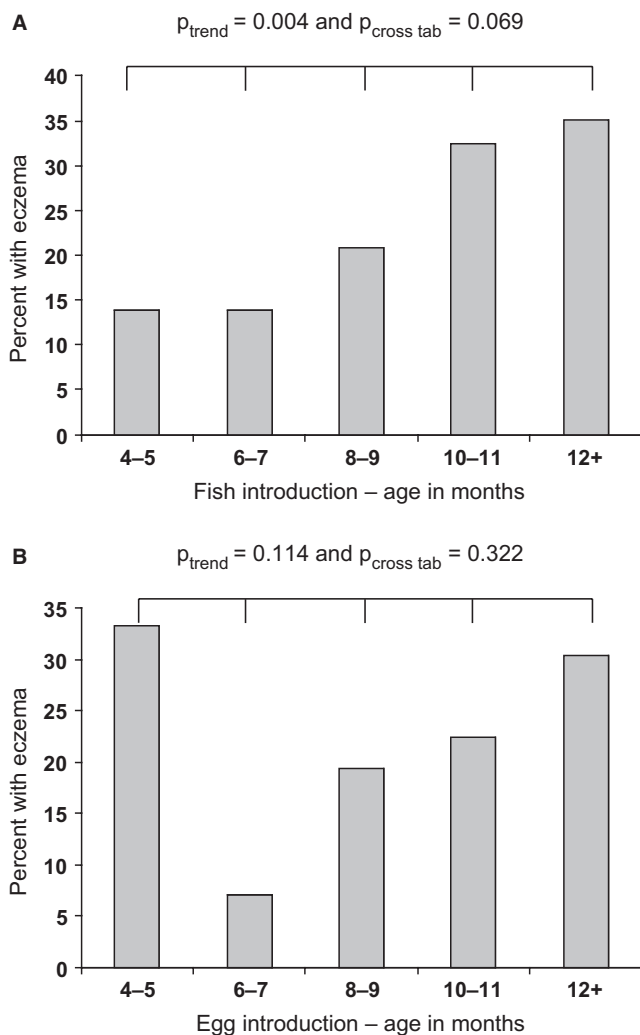
		Exclusive breastfeeding Median (25th, 75th)	Partial breastfeeding Median (25th, 75th)	Cow's milk products* Median (25th, 75th)	Fruit Median (25th, 75th)	Solids† Median (25th, 75th)	Fish Median (25th, 75th)	Egg Median (25th, 75th)
Eczema	No	4 (3.9, 4.5)	7.2 (4.0, 10.0)	5 (4.0, 6.0)	5 (4.0, 5.0)	4 (4.0, 4.6)	8 (6.0, 11.0)	11 (9.0, 13.0)
	Yes	4 (3.2, 4.5)	6.7 (6.0, 9.0)	5 (4.0, 7.0)	5 (4.0, 5.0)	4 (4.0, 5.0)	11 (8.0, 13.0)	13 (10.0, 13.0)
		p = 0.634	p = 0.818	p = 0.996	p = 0.859	p = 0.971	p = 0.004	p = 0.070
Asthma	No	4 (3.5, 4.5)	7 (4.5, 9.0)	5 (4.0, 6.0)	5 (4.0, 5.0)	4 (4.0, 4.5)	9 (6.0, 12.0)	11 (9.0, 13.0)
	Yes	4 (4.0, 5.1)	7.2 (4.8, 10.1)	7 (4.8, 10.0)	5 (4.4, 6.1)	4.2 (4.0, 5.1)	13 (7.9, 13.0)	13 (12.2, 13.0)
		p = 0.507	p = 0.777	p = 0.092	p = 0.296	p = 0.289	p = 0.129	p = 0.079
Food allergy	No	4 (4.0, 4.5)	7 (4.5, 9.0)	5 (4.0, 6.0)	5 (4.0, 5.0)	4 (4.0, 5.0)	9 (6.0, 12.0)	11 (9.0, 13.0)
	Yes	4 (3.3, 4.0)	8.5 (5.5, 10.1)	13 (6.5, 13.0)	5 (4.0, 5.0)	4 (4.0, 4.2)	13 (9.8, 13.0)	13 (13.0, 13.0)
		p = 0.380	p = 0.248	p = 0.001	p = 0.885	p = 0.860	p = 0.010	p = 0.075
Sensitization	No	4 (4.0, 4.5)	7 (4.7, 10.0)	5 (4.0, 6.5)	5 (4.0, 5.0)	4 (4.0, 5.0)	9 (6.0, 12.0)	11 (9.0, 13.0)
	Yes	4 (2.5, 4.5)	7 (4.0, 9.0)	5 (4.0, 6.0)	5 (4.0, 5.0)	4 (4.0, 5.0)	9.5 (6.0, 13.0)	13 (10.0, 13.0)
		p = 0.582	p = 0.408	p = 0.488	p = 0.878	p = 0.836	p = 0.275	p = 0.300

Ages are given in median months. 25th and 75th percentiles are given within brackets.

Mann-Whitney Tests were used to compare differences between groups.

*All types of cow's milk products including infant formula.

†Potatoes, root vegetables, vegetables and meat.



but no association was found ($p = 0.552$, Median test). To further control for confounding factors, we performed a multiple logistic regression analysis controlling for maternal and paternal history of allergy, as well as ongoing breastfeeding at 6 months of age. Still, the association between late fish introduction and eczema remained, OR 1.16 (95% CI 1.02–1.33, $p = 0.026$), i.e. a 16% increased prevalence of eczema for every 2 months that introduction of fish was delayed.

Furthermore, eczema development between 6 and 12 months of age was associated with the timing of fish introduction. In children with no history of eczema at 6 months of age, to whom fish were introduced during this time period, 2% (2/107) reported eczema at 12 months. If fish introduction was introduced after 12 months of age, the corresponding figure was 18% (8/44) ($p < 0.001$). In children already having eczema at 6 months of age, the timing of fish introduction did not influence the frequency of eczema at 12 months (data not shown).

We also tested if there were any correlations between the age when fish was introduced and eosinophil counts and total IgE-levels in blood at 18 months of age. No such correlations were, however, seen ($r = 0.143$, $p = 0.104$ and $r = 0.031$, $p = 0.680$, respectively).

The introduction of cow's milk was postponed in food-allergic children, but not in children with eczema, asthma or sensitization. Cow's milk-based products were, however, introduced at a median age of 4.6 months in children with parent-reported gastrointestinal symptoms, when

Figure 1 Frequency of eczema in relation to age in months when fish (A) and hen's egg (B) were introduced into the child's diet. p-values are given for trend (p_{trend}) and cross tabulation ($p_{\text{cross tab}}$), Monte Carlo method.

Table 4 Duration of breastfeeding, and age in months when different food items were introduced, in relation to possible confounding factors

		Exclusive breastfeeding Median (25th, 75th)	Partial breastfeeding Median (25th, 75th)	Cow's milk products* Median (25th, 75th)	Fruit Median (25th, 75th)	Solids [†] Median (25th, 75th)	Fish Median (25th, 75th)	Egg Median (25th, 75th)
Maternal history of allergy	No	4 (4.0, 4.5)	7 (5.0, 9.0)	5 (4.0, 6.0)	5 (4.0, 5.0)	4 (4.0, 5.0)	9.5 (6.0, 11.5)	10 (9.0, 13.0)
	Yes	4 (3.5, 5.0)	7.2 (4.3, 9.6)	5 (4.0, 7.0)	5 (4.0, 5.0)	4 (4.0, 5.0)	10 (6.0, 13.0)	13 (10.0, 13.0)
		p = 0.205	p = 0.707	p = 0.578	p = 0.302	p = 0.343	p = 0.079	p = 0.015
Paternal history of allergy	No	4 (3.6, 4.9)	7.2 (4.5, 9.0)	5.8 (4.0, 6.9)	5 (4.0, 5.0)	4 (4.0, 5.0)	9.5 (6.0, 12.0)	11.2 (9.0, 13.0)
	Yes	4 (3.5, 4.5)	7 (5.0, 10.0)	5 (3.0, 6.0)	5 (4.0, 5.0)	4 (4.0, 4.5)	10 (6.0, 13.0)	12 (10.0, 13.0)
		p = 0.675	p = 0.925	p = 0.045	P = 0.452	p = 0.598	p = 0.567	p = 0.393
Breastfeeding for at least 6 months	No	2 (0.5, 4.0)	4.5 (4.5, 9.0)	4 (2.0, 5.0)	4.5 (4.0, 5.0)	4 (4.0, 4.0)	9.5 (5.5, 13.0)	11 (9.0, 13.0)
	Yes	4 (4.0, 5.0)	8.0 (6.5, 10.0)	5.2 (4.6, 7.0)	5 (4.1, 5.0)	4 (4.0, 5.0)	10 (6.0, 12.0)	11.7 (9.0, 13.0)
		p < 0.001	p < 0.001	p < 0.001	p = 0.001	p = 0.001	p = 0.184	P = 0.614
Wheeze reported during first 6 months	No	4 (4.0, 4.5)	7 (5.0, 9.0)	5 (4.0, 6.0)	5 (4.0, 5.0)	4 (4.0, 5.0)	10 (6.0, 13.0)	12 (9.0, 13.0)
	Yes	4 (2.0, 4.5)	6.7 (4.5, 10.5)	5 (4.0, 7.0)	5 (4.1, 5.9)	4.2 (4.0, 4.9)	8 (5.6, 12.2)	10.7 (9.2, 13.0)
		p = 0.431	p = 0.911	p = 0.681	p = 0.111	P = 0.471	p = 0.246	p = 0.771
Eczema reported during first 6 months	No	4 (4.0, 4.5)	7 (4.5, 9.0)	5 (4.0, 6.0)	5 (4.0, 5.0)	4 (4.0, 5.0)	9.5 (6.0, 12.0)	11.2 (9.0, 13.0)
	Yes	4 (3.0, 4.5)	8 (6.0, 9.5)	5 (4.0, 6.5)	5 (4.0, 5.0)	4 (4.0, 5.0)	11 (8.0, 13.0)	13 (9.0, 13.0)
		p = 0.402	p = 0.619	p = 0.615	p = 0.969	p = 0.835	p = 0.194	p = 0.484
Milk reaction reported during first 6 months [‡]	No	4 (4.0, 4.5)	7 (4.6, 9.0)	5 (4.0, 4.6)	5 (4.0, 4.5)	4 (4.0, 4.6)	9.5 (6.0, 12.0)	11 (9.0, 13.0)
	Yes	4 (2.0, 4.0)	8 (4.0, 10.1)	13 (7.5, 13.0)	5 (4.2, 5.0)	4 (4.0, 5.0)	13 (9.0, 13.0)	13 (11.0, 13.0)
		p = 0.108	p = 0.354	p < 0.001	p = 0.951	p = 0.567	p = 0.006	p = 0.040

Ages are given in median months. 25th and 75th percentiles are given within brackets.

Mann-Whitney Tests were used to compare differences between groups.

*All types of cow's milk products including infant formula.

[†]Potatoes, root vegetables, vegetables and meat.

[‡]Adverse reaction to cow's milk reported during first 6 months of life.

compared to 5 months in children without such symptoms ($p = 0.04$).

Fruits and solids were introduced at similar ages independent of health status. The duration of breastfeeding was no different in sensitized children, or in children with allergic disease, when compared to healthy children.

DISCUSSION

In this study, we examined whether the development of allergic diseases during the child's first 18 months of life was associated with the time at which different food items were introduced. We found that introduction of fish into the child's diet seemed to protect against eczema development, but that it did not affect those who already had eczema. Furthermore, there was also a 'dose-response' effect in that the protection on a group-level was greater the earlier fish was introduced into the diet, because very few children developed eczema after the introduction of fish.

Our results, with prospectively collected exposure data and diagnostic labelling based on clinical examination, support previous questionnaire-based results that early introduction of fish into the child's diet may protect against allergy development (9–11). Selection bias may, however, influence these types of relationships. But we found no support for such an explanation, because the negative association between fish in the diet and eczema remained in all steps controlling for reversed causation and selection bias.

The allergy-protective effect of early fish introduction is, however, not easy to explain, and all aspects of 'allergic disease' may not be similarly affected. We only found a protective effect on eczema development, but it does not necessarily mean that the allergy-protective effect of fish is restricted to skin inflammation. We found a similar numeric association between the timing of fish introduction and asthma development, but the number of asthma cases was too few to reach statistical significance. The effect on food allergy was not possible to interpret in this context, because we had to exclude the food-allergic children from the analysis in order to control for reversed causation. Allergic rhinitis was not analysed as an outcome variable, because the disease is very rare in this age group.

The underlying mechanisms involved in this allergy-protective effect of fish can only be speculated upon. Fish, with its rich content of long-chain omega-3 fatty acids such as docosahexaenoic acid and eicosapentaenoic acid, may have immunoregulatory and/or anti-inflammatory properties. Protective effects of omega-3 fatty acids on allergic diseases have been seen in some studies (15–18), whereas others found no such associations (19) and the allergy-protective effect from a rich food content of omega-3 is not very convincing (20). Fish is also rich in fat-soluble vitamins A and D (Swedish National Food Administration), and vitamin D has in some recent studies been associated with less allergy (21–25), although this is not compatible with historic observations, and conflicts with some recent studies (26–28),

suggesting that the association between fish and eczema or allergy prevention might not be a simple D vitamin effect.

Sensitization was not associated with the timing of fish introduction in our study, despite a reasonable number of cases analyses. Having in mind the older age of the children in the study of Kull et al. (10), this finding is to some extent in contrast to the results in that study, but in concordance with a recent study in mice. (29) In mice, fish oil-enriched food reduces the production of Th1 cytokines, but does not decrease Th2-mediated sensitization and respiratory hypersensitivity. It is possible that fish-induced allergy protection is more pronounced in diseases that also include a Th1-response, as in eczema (30).

In contrast to fish, no other food items or feeding patterns showed any major or significant influence on allergy development.

The small size of the study is its main weakness. Lack of associations may be because of Type II errors. On the other hand, the size of the study is also its strength, because it made it possible to use a very detailed and structured follow-up. Diaries were used by the parents, and structured interviews were conducted every 6th month. Children with signs and symptoms suggestive of allergic disease were seen by a paediatric allergist or gastroenterologist at a tertiary centre within a few days, and the diagnoses were all based on structured clinical evaluation and strict predefined criteria.

In conclusion, early introduction of fish into the child's diet was associated with less eczema development, and a tendency to less asthma. Sensitization was, however, not affected by the timing of fish introduction.

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