Early introduction of fish decreases the risk of eczema in infants

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ABSTRACT

Background: Atopic eczema in infants has increased in western societies. Environmental factors and the introduction of food may affect the risk of eczema.

Aims: To investigate the prevalence of eczema among infants in western Sweden, describe patterns of food introduction and assess risk factors for eczema at 1 year of age.

Methods: Data were obtained from a prospective, longitudinal cohort study of infants born in western Sweden in 2003; 8176 families were randomly selected and, 6 months after the infant’s birth, were invited to participate and receive questionnaires. A second questionnaire was sent out when the infants were 12 months old. Both questionnaires were completed and medical birth register data were obtained for 4921 infants (60.2% of the selected population).

Results: At 1 year of age, 20.9% of the infants had previous or current eczema. Median age at onset was 4 months. In multivariable analysis, familial occurrence of eczema, especially in siblings (OR 1.87; 95% confidence interval (CI) 1.50 to 2.33) or the mother (OR 1.54; 95% CI 1.30 to 1.84), remained an independent risk factor. Introducing fish before 9 months of age (OR 0.76; 95% CI 0.62 to 0.94) and having a bird in the home (OR 0.35; 95% CI 0.17 to 0.75) were beneficial.

Conclusions: One in five infants suffer from eczema during the first year of life. Familial eczema increased the risk, while early fish introduction and bird keeping decreased it. Breast feeding and time of milk and egg introduction did not affect the risk.

Eczema in infants is a common health problem throughout the world, although the incidence varies.1 However, heredity is known to exert a major influence,2 and food and the period of food introduction may have an effect on age at onset and the severity of the disease.

There has been a substantial increase in the prevalence of allergic diseases in recent decades,1 4 but the reasons for this are still unknown despite intensive research. The low prevalence of allergy in Eastern Europe was thought to be due to a difference in intestinal flora.5 In addition, data from experimental animal studies suggest that early contact with allergens might provide protection from subsequent sensitisation,6 which is also supported by epidemiological findings.7 However, other studies report different results.8

There is consensus that parental tobacco smoking plays an important role in the occurrence of early wheezing, but the influence on eczema is disputed.9 10 Dairy products,11 omega-3 fatty acids13 and a diet containing lactobacilli14 have been suggested to be protective factors against the development of atopy.

The aims of this study were to investigate the current prevalence of eczema among infants in western Sweden, to describe current patterns of food introduction and to assess the risk factors for eczema at 1 year of age.

METHODS

“Infants of Western Sweden” is an ongoing study in western Sweden. The region has 1.5 million inhabitants (one sixth of the Swedish population) and consists of urban, rural and coastal areas. Gothenburg, with 500 000 inhabitants, is the largest city.

From the total birth cohort of 16 682 infants born in the region in 2003, 8176 families (50%) were randomly selected.15 When the infant was 6 months of age, the family was sent an invitation and a questionnaire (Q1) which sought detailed information on the family, environment, perinatal history, tobacco, breast feeding, food introduction and diseases in the first year, with special reference to allergic diseases. Families willing to participate returned written informed consent together with the questionnaire. These families were then sent a second questionnaire (Q2) when the child was 12 months of age. Q1 was sent out to 8176 families and completed by 5605, giving a response rate of 68.5%. Of these 5605 families, 4941 also completed Q2 (88.2% of those who answered Q1). Medical birth register data were available for 4921 (99.6%) of these 4941 (60.2% of the originally selected population). Details relating to the questionnaires have previously been published.16 17
The question on eczema was: “Has your child had eczema? (y/n)”, while that on food allergy was: “Has your child a diagnosis of food allergy from a doctor? (y/n)”. Food frequency data were collected at 6 and 12 months.

In the statistical analysis of eczema, 2×2 tables with the χ² test and binary logistic regression were used and risks were estimated using odds ratios (OR) with 95% confidence intervals (CI). Factors that were significant with a p value of <0.01 in the univariable analysis were then analysed in a multivariable model. Secondary (disease-associated) variables were excluded and further adjustment was carried out for “atopic reasons” for not having furry animals in the home (manifest allergy or fear of allergy), plus cow’s milk allergy. The SPSS statistical package v 15.0 was used for calculations.

The study was approved by the ethics committee at the University of Gothenburg.

Table 1 Reported prevalence of eczema, diagnosed food allergy, pet keeping and dietary factors in infants in western Sweden in 2004–2005: the Infants of Western Sweden Study

|                               | n (%)   |
|-------------------------------|---------|
| **Eczema** (n = 4953)         |         |
| At 6 months                   | 692 (13.9) |
| At 12 months                  | 1033 (20.9) |
| **Food allergy** (n = 4944)   |         |
| Any food allergy              | 241 (4.9) |
| Cow’s milk                    | 194 (3.9) |
| Eggs                          | 126 (2.5) |
| Fruit or vegetables           | 41 (0.83) |
| Cereals                       | 18 (0.36) |
| Fish                          | 14 (0.28) |
| Soy protein                   | 12 (0.24) |
| Peanuts                       | 10 (0.20) |
| Peas                          | 9 (0.18)  |
| Nuts or almonds               | 8 (0.16)  |
| **Pets in the home** (n = 4987) |         |
| Cat                           | 1076 (21.6) |
| Dog                           | 729 (14.6) |
| Rodent                        | 162 (3.2)  |
| Bird                          | 113 (2.3)  |
| **Main type of fat on bread** (n = 4893) |         |
| Butter                        | 3488 (71.3) |
| Margarine                     | 1164 (23.8) |
| Nilt                          | 241 (4.9)  |
| **Frequency of lactic acid** (yoghurt, fermented vegetables, etc) in the diet (n = 4929) |         |
| 3+ Times/week                 | 2497 (50.7) |
| 1–3 Times/week                | 1439 (29.2) |
| 1–3 Times/month               | 531 (10.8)  |
| Occasionally                  | 161 (3.3)  |
| Never                         | 301 (6.1)  |
| **Frequency of fish consumption** (n = 4953) |         |
| 3+ Times a week               | 250 (5.0)  |
| 1–3 Times a week              | 2995 (60.5) |
| 1–3 Times a month             | 1296 (26.2) |
| A few times a year            | 217 (4.4)  |
| Never                         | 195 (3.9)  |
| **Type of fish usually consumed** (n = 4473) |         |
| Lean fish (cod, haddock)      | 3516 (78.6) |
| Salmon                        | 772 (17.3)  |
| Flattfish                     | 140 (3.1)  |
| Mackerel or herring           | 45 (1.0)   |

RESULTS

Eczema
At 6 months of age, 13.9% of families said that their infant had previous or current eczema, while the corresponding figure at 12 months was 20.9% (table 1). The median age at onset was 4 months (mean age 5.4 months).

Food allergy
Food allergy had been diagnosed by a physician in 4.9% of the study population (table 1).

Furry pets
Many families had furry pets. The most common was a cat (21.6%), followed by a dog (14.6%) and rodents (3.2%). The keeping of pets was more common in rural than in urban areas. For example, dogs were kept by 8.4% of the households in the city of Gothenburg, while the figures were 25.8% and 20.7% in the counties of Dalsland and Skaraborg, respectively.

Breast feeding and food introduction
Breast feeding and timing of the introduction of cow’s milk protein, cereals and solids are described in figs 1 and 2. At the age of 16 weeks, more than 80% of the infants were breast fed, while one third were exclusively breast fed (no cow’s milk protein introduced) (fig 1). At the age of 6 months, two thirds were still breast fed and 10% were exclusively breast fed. At about 30 weeks, 50% of the infants had been weaned (fig 1).

The median age for the introduction of cow’s milk protein was 9 weeks, compared with 18 weeks for the introduction of solids and 22 weeks for cereals (fig 2).

Fish was introduced at a median age of 7 months and eggs at a median age of 9 months (fig 2).

Butterfat was used on bread by 71.5% of the families at 12 months, while 50.7% consumed fermented dairy products (table 1) more than three times a week. When they ate fish, 18.3% mainly consumed fat fish such as salmon.

Risk factors for eczema at 1 year
Univariable analysis
The variables significant at p<0.01 are presented in table 2. The non-significant variables with a p value between 0.01 and 0.05 as well as those with a p value ≥0.05 are listed in the footnote.

Multivariable analysis
In the multivariable analysis, significant risk factors were maternal eczema, a sibling with eczema, a bird in the home, the introduction of fish before 9 months of age and cow’s milk allergy (table 3).

Since breast feeding and smoking were non-significant (p>0.01) in the univariable analysis they were not included in the final multivariable model. However, since the effects of breast feeding and smoking on allergic disease are debated, we also carried out an analysis including these factors in the model. This confirmed that they were not statistically significant risk factors.

DISCUSSION
This study shows that one in five infants have eczema during the first year of life and, as expected, there is a strong association with a family history of eczema. Furthermore, we found beneficial effects from introducing fish before 9 months of age, while short duration of breast feeding, keeping furry pets
Since smoking is associated with our study. On the other hand, opinions differ as to whether furry pets. We found a prevalence of 21% of eczema among infants. Food habits among infants: introduction of cow’s milk protein, cereals, solids, eggs and fish in western Sweden, 2003–2004.

Figure 1  Prevalence of exclusive breast feeding and any breast feeding during the first year of life in western Sweden, 2003–2004.

Figure 2  Food habits among infants: introduction of cow’s milk protein, cereals, solids, eggs and fish in western Sweden, 2003–2004.

Since birds almost always are kept inside providing continuous indoor exposure, it may be that birds promote exposure to endotoxin. This might explain why we found a protective effect of bird keeping.

Previous primary preventive advice in Sweden recommended the delayed introduction of eggs and fish to infants with strong allergic heredity. Although this advice was abandoned in the autumn of 2002 because supportive evidence was lacking, we found that many parents waited to introduce eggs and fish. The results of our study show that outdated primary preventive advice which lacks evidence tends to be still followed by the general population. At the time of the study, allergy prevention advice placed no restrictions on the consumption of eggs or fish either in families at risk or in the rest of the population.

The results suggest that advice previously given at infant welfare clinics concerning the introduction of small portions of cereals and solids at 4 months of age is being followed, while cow’s milk-based formulas and weaning foods are introduced earlier by many parents. The WHO code advocating exclusive breast feeding up to 6 months of age has been recommended in Sweden since 2001. The early steep rise in the curve showing the introduction of cow’s milk (fig 2) could be explained by the parents (truthfully) counting every small helping of formula, for example during the neonatal period before the firm establishment of breast feeding.

In our study, the strongest risk factor for eczema was a family history of eczema and maternal eczema in particular. Our finding that a family history of eczema is a stronger risk factor than a family history of other atopic diseases is compatible with, for example, the ALSPAC study, where parental eczema was regarded as a better marker than parental asthma or hay fever. In fact, a Danish twin study found that genes accounted for 82% of individual susceptibility, while non-shared environmental factors accounted for 18%. Recently, it has been demonstrated that loss-of-function mutations in the filaggrin gene predispose to eczema. Filaggrin is a key protein of the epidermis that has an important role in the formation of the skin barrier. Loss of filaggrin function seems to play a role both in the pathogenesis of eczema and the subsequent progression of atopy.
In the multivariable analysis, we found that the introduction of fish before 9 months of age had a protective effect on eczema. This is compatible with the findings of Kull et al.\textsuperscript{21} who found that regular fish consumption in the first year of life was associated with a lower risk of eczema at 4 years of age. It has been suggested that a high ratio of omega-6 to omega-3 fatty acids, as is common in western diets, could contribute to the pathogenesis of allergic disease.\textsuperscript{22} The fact that fish is rich in omega-3 fatty acids could partly explain the effects found in this cohort. However, we found no influence of the type of fish ingested (lean/white or fat/oily) in this study, which is compatible with the CAPS study\textsuperscript{10} and recent data from Norway.\textsuperscript{24} The Norwegian study reported beneficial effects on the risk of developing allergic disease if the child ate fish, especially lean fish, but neither the CAPS nor the Norwegian study found that omega-3 fatty acids reduced the risk of allergic disease, including eczema. This makes it somewhat difficult to ascribe the effect to omega-3 fatty acids only.

### Table 2

| Risk factor                                | Eczema n (%) | No eczema n (%) | OR (95% CI)     | p Value  |
|--------------------------------------------|--------------|-----------------|-----------------|----------|
| Paternal asthma                            | 108 (10.5)   | 280 (7.2)       | 1.51 (1.20 to 1.91) | 0.001    |
| Maternal rhinoconjunctivitis               | 320 (31.3)   | 833 (21.5)      | 1.66 (1.42 to 1.93) | <0.001   |
| Paternal rhinoconjunctivitis               | 287 (28.0)   | 876 (22.6)      | 1.33 (1.14 to 1.56) | <0.001   |
| Sibling with rhinoconjunctivitis           | 68 (6.6)     | 179 (4.6)       | 1.47 (1.10 to 1.96) | 0.009    |
| Maternal eczema                            | 392 (38.3)   | 917 (25.7)      | 2.00 (1.73 to 2.31) | <0.001   |
| Paternal eczema                            | 214 (20.9)   | 569 (14.7)      | 1.53 (1.29 to 1.83) | <0.001   |
| Sibling with eczema                        | 209 (20.4)   | 436 (11.3)      | 2.02 (1.69 to 2.43) | <0.001   |
| Living in an urban area                    | 631 (62.5)   | 2134 (56.0)     | 1.31 (1.14 to 1.51) | <0.001   |
| Maternal medication during pregnancy       | 328 (32.2)   | 1066 (27.7)     | 1.24 (1.07 to 1.44) | 0.005    |
| Light sleeper at 6 months                  | 321 (31.3)   | 1016 (26.2)     | 1.28 (1.10 to 1.49) | 0.001    |
| Troubled sleep at 6 months                 | 150 (14.6)   | 434 (11.2)      | 1.36 (1.11 to 1.66) | 0.003    |
| 3+ Awakenings per night                    | 215 (21.8)   | 657 (17.7)      | 1.30 (1.09 to 1.54) | 0.003    |
| Male gender                                | 574 (56.1)   | 1979 (51.1)     | 1.22 (1.06 to 1.40) | 0.005    |
| Dog at home                                | 123 (11.9)   | 599 (15.3)      | 0.75 (0.61 to 0.92) | 0.006    |
| Bird at home                               | 12 (1.2)     | 100 (2.6)       | 0.45 (0.25 to 0.82) | 0.009    |
| Age at introduction of fish                |              |                 |                 | <0.001   |
| 0–2 Months                                 | 6 (0.7)      | 15 (0.4)        | 1.1 (0.4 to 2.9)  | 0.83     |
| 3–5 Months                                 | 194 (21.3)   | 750 (20.9)      | 0.7 (0.6 to 0.9)  | 0.003    |
| 6–8 Months                                 | 462 (50.8)   | 2142 (59.6)     | 0.6 (0.5 to 0.7)  | <0.001   |
| 9–12 Months                                | 248 (27.3)   | 689 (19.2)      | 1 (Ref)           | Ref      |
| Type of fat on bread                       |              |                 |                 | 0.003    |
| Dairy                                      | 674 (67.2)   | 2794 (72.3)     | 1 (Ref)           | Ref      |
| Margarine                                  | 280 (27.9)   | 878 (22.7)      | 1.32 (1.13 to 1.55) | 0.001    |
| NIl                                        | 49 (4.9)     | 191 (4.9)       | 1.06 (0.77 to 1.47) | 0.71     |
| Frequency of fish consumption              |              |                 |                 | <0.001   |
| 3+ Times a week                            | 54 (5.3)     | 195 (5.0)       | 1 (Ref)           | Ref      |
| 1–3 Times a week                           | 584 (57.0)   | 2400 (61.6)     | 0.88 (0.64 to 1.20) | 0.42     |
| 1–3 Times a month                          | 247 (24.1)   | 1038 (26.6)     | 0.86 (0.62 to 1.20) | 0.37     |
| A few times a year                         | 57 (5.6)     | 156 (4.0)       | 1.32 (0.86 to 2.02) | 0.20     |
| Never                                      | 83 (8.1)     | 110 (2.9)       | 2.73 (1.80 to 4.13) | <0.001   |
| Usually eats lean fish                     | 723 (79.3)   | 2918 (82.5)     | 0.81 (0.68 to 0.97) | 0.025    |
| Frequency of lactic acid (yoghurt, fermented vegetables, etc) in diet | | | | <0.001 |
| 3+ Times a week                            | 497 (49.8)   | 1968 (51.1)     | 1 (Ref)           | Ref      |
| 1–3 Times a week                           | 257 (25.2)   | 1173 (30.2)     | 0.88 (0.75 to 1.04) | 0.12     |
| 1–3 Times a month                          | 110 (10.8)   | 419 (10.8)      | 1.05 (0.83 to 1.32) | 0.69     |
| A few times a year                         | 29 (2.8)     | 131 (3.4)       | 0.89 (0.59 to 1.34) | 0.56     |
| Never                                      | 125 (12.3)   | 174 (4.5)       | 2.87 (2.24 to 3.69) | <0.001   |
| Troubled sleep at 12 months                | 203 (19.7)   | 611 (15.6)      | 1.32 (1.11 to 1.58) | 0.002    |

### Table 3

| Risk factor                                | OR (95% CI)     | p Value  |
|--------------------------------------------|-----------------|----------|
| Maternal eczema                            | 1.54 (1.30 to 1.84) | <0.001   |
| Sibling with eczema                        | 1.87 (1.50 to 2.33) | <0.001   |
| Bird in the home                           | 0.35 (0.17 to 0.75) | 0.007    |
| Introduction of fish before 9 months       | 0.76 (0.62 to 0.94) | 0.009    |
| Cow’s milk allergy                         | 3.64 (2.35 to 5.64) | <0.001   |
Dairy products have also been suggested to have beneficial effects on allergic disease. In a study from the Netherlands, it has been shown that milk and butter consumption reduced the risk of asthma.32 However, we were not able to demonstrate any protective effects by dairy products in this study.

The results concerning a possible protective effect on eczema by breast feeding are contradictory. Kull et al26 found a protective effect by breast feeding on eczema at 4 years of age and protective effects have also been reported in other studies.36 37 However, in this study we did not find that breast feeding had any protective effect on the occurrence of eczema. This is in line with the results of Belgian PIPO, the Dutch KOALA and the Australasian CAPS studies.3 19 38

There are also a few studies that claim that prolonged breast feeding can increase the prevalence of eczema.39 40 This may possibly be due to reverse causation, as infants with manifest eczema tend to be breast fed longer than other infants. However, the CAPS study found no significant association between the presence of eczema at 4 weeks and at 3 months and continued breastfeeding beyond those dates. Nor did we find any effects on the prevalence of eczema from parental smoking during or after pregnancy, which is in line with the PIPO study.4

In conclusion, we have found that one in five infants in western Sweden have eczema. In a multivariable analysis, we found large effects from heredity and no effect from the duration of breast feeding or the age at which milk or eggs were introduced, while protective effects from introducing fish before 9 months were found.

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