COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

REVIEW OF ADVICE ON PEANUT AVOIDANCE

2.1 Summary of three selected recent review papers and one editorial, on exposure to food allergens in early life and risk of later development of asthma and atopic dermatitis (atopic eczema)

2.2 Summary of evidence from literature search (March 2006 to present) on evidence on early exposure to food allergens and later development of non-food allergic outcomes.

2.3 Full text papers summarised in section 2.1

2.4 Abstracts of fifteen papers summarised in section 2.2

Secretariat
October 2008
2.1: Summaries of three selected recent review papers and one editorial, on exposure to food allergens in early life and risk of later development of asthma, wheeze and atopic dermatitis (atopic eczema)

**Paper 1 (review): Maternal dietary antigen avoidance during pregnancy or lactation, or both, for preventing or treating atopic disease in the child (Review).**

Summary:
This Cochrane systematic review aimed to assess the effects of prescribing an antigen avoidance diet during pregnancy or lactation, or both, on maternal and infant nutrition and on the prevention or treatment of atopic disease in the child by searching the Cochrane Trials Register to identify relevant trials published up to March 2006. Randomized or quasi-randomized comparisons of maternal dietary antigen avoidance prescribed to pregnant or lactating women were included. Trials of multimodal interventions that included manipulation of the infant’s diet other than breast milk or of non-dietary aspects of the infant’s environment were excluded. Data from four trials were included in the review.

The authors concluded that “prescription of an antigen avoidance diet to a high-risk woman during pregnancy or lactation is unlikely to reduce substantially her risk of giving birth to an atopic child and may have an adverse effect on maternal or fetal nutritional status, or both. Prescription of an antigen avoidance diet to a high-risk woman during lactation may reduce her child’s risk of developing atopic eczema, but better trials are needed”.

**Paper 2 (review) : Effects of early nutritional interventions on the development of atopic disease in infants and children: The role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas.**
Greer, FR. Sicherer, SH. Burks, W. and the Committee on Nutrition and Section on Allergy and Immunology. (2008) Pediatrics. 121:1 183-191

Summary:
This is a clinical review report on the effects of early nutritional interventions on the development of atopic disease in infants and children, which replaces an earlier policy statement from the American Academy of Pediatrics (AAP) published in 2000. The clinical report focuses on the role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolysed formulas in the prevention or delay of atopic dermatitis, asthma and food allergy in childhood.

When considering the whole body of published evidence, the AAP concluded that “it is evident that inadequate study design and/or paucity of data currently limit the ability to draw firm conclusions about certain aspects of atopy prevention through dietary prevention. In some circumstances, in which there are insufficient studies, the lack of proven efficacy does not indicate that the approach is disproved. Rather, more studies would be needed to clarify whether there is a positive or negative effect on atopy outcomes.”
The following statements are the conclusions of the AAP on those areas of evidence which are directly linked to the issue currently under consideration by the COT:

**Association between maternal dietary restrictions and development of atopic disease:**
1. “At the present time, there is a lack of evidence that maternal dietary restrictions during pregnancy play a significant role in the prevention of atopic disease in infants. Similarly, antigen avoidance during lactation does not prevent atopic disease, with the possible exception of atopic eczema, although more data are needed to substantiate this conclusion.”

**Association between breastfeeding and cows’ milk formula feeding and development of atopic disease.**
2. “For infants at high risk of developing atopic disease, there is evidence that exclusive breastfeeding for at least 4 months compared with feeding intact cow milk protein formula decreases the cumulative incidence of atopic dermatitis in the first 2 years of life.”
3. “There is evidence that exclusive breastfeeding for at least 3 months protects against wheezing in early life. However, in infants at risk of developing atopic disease, the current evidence that exclusive breastfeeding protects against allergic asthma occurring beyond 6 years of age is not convincing.”
4. “There is no convincing evidence for the use of soybased infant formula for the purpose of allergy prevention.”

**Association between timing of introduction of complementary feeding and development of atopic disease:**
5. “Although solid foods should not be introduced before 4 to 6 months of age, there is no current convincing evidence that delaying their introduction beyond this period has a significant protective effect on the development of atopic disease regardless of whether infants are fed cow milk protein formula or human milk. This includes delaying the introduction of foods that are considered to be highly allergic, such as fish, eggs, and foods containing peanut protein.”

In general, the AAP states that “for infants after 4-6 months of age, there are insufficient data to support a protective effect of any dietary intervention for the development of atopic disease.”

**Paper 3 (editorial) : Maternal and infant diets for prevention of allergic diseases: understanding menu changes in 2008.**

Summary: This editorial reviews the updated 2008 AAP clinical report (summarised above) and compares the report and the statements made within it to previous dietary recommendations made by the AAP and from other professional societies. The authors state that the paper is not an attempt at an extensive review of the subject areas, but it does however comment on pertinent studies published since the 2008
AAP clinical report. The authors highlight that a major difference of the revised AAP report is that “statements about possible dietary changes are made along with the evidence (or lack thereof) about efficacy” rather than making dietary recommendations, and explain that this approach is more sensitive to the notion that when evidence is unclear, physicians and patients would be aware of those caveats. The authors seek to clarify and draw out the key conclusions of the 2008 AAP report.

**Paper 4 (review): Systematic review of the relationship between early introduction of solids to infants and development of allergic disease.**

**Summary:**
This systematic review includes 13 studies which had investigated whether early solid feeding (before 4 months of age) increases the risk of allergic disease (encompassing eczema, asthma or wheeze, food allergy, allergic rhinitis, pollen allergy and animal dander allergy). The authors report that this is the first systematic review of evidence in this area.

The authors conclude that “the evidence that introduction of solid food to infants before 4 months of age increases the risk of allergic disease is conflicting and inconsistent……there is a consistent association between the persistence of eczema and the introduction of solid foods before 4 months of age that is supported by long term follow-up studies and the dose-dependant nature of the association. However, “there is insufficient evidence to suggest that, on it’s own, the early introduction of solids to infants is associated with an increased risk of asthma”. The authors highlight that many of the included studies lacked rigorous design, citing recall bias, lack of controlled study design, failure to adjust for confounders, lack of blinding to feeding history and outcome misclassification as problems with study methodologies. The authors suggest that additional controlled trials are needed to help guide physicians as they advise parents about the allergic risks of early introduction of solids.

**Secretariat**
**October 2008**
2.2: Summary of published literature from March 2006 to present on exposure to food allergens in early life and risk of later development of atopic disease in childhood.

The literature search was conducted in OVID Medline supplemented through consultation with the four scientific experts who have been assisting the COT in this review and have expert knowledge of the literature in this area. Fifteen studies of relevance (published since March 2006) have been identified and have been categorised into the following areas of evidence:

1.) Maternal dietary exposure to food allergens and development of atopic disease in childhood;
2.) Early life feeding practices and development of atopic diseases in childhood;
3.) Multifaceted interventions to reduce the risk of atopic disease (including dietary maternal and early life exposure to, or avoidance of, food allergens).

Studies which have looked exclusively at the role of breastfeeding or formula feeding on development of atopic disease were not considered.

Summary of literature on maternal dietary exposure to food allergens and development of atopic disease in childhood

Four studies have been identified which have aimed to investigate the role of diet during pregnancy of development of atopic disease in childhood (Sausenthaler (2007), Willers (2007), Willers (2008) and Romieu (2007). All included studies report on general population cohorts. No randomised controlled trials have been conducted. Three out of the four studies identified report findings when analysing a complete dietary pattern during pregnancy, whereas Romieu (2007) has investigated the effect of consumption of one food (fish) during pregnancy. Statistically significant findings involving exposure to, or avoidance of, allergenic foods and development of asthma, wheeze or eczema have been reported below.

No studies were identified which have investigated the role of exposure to allergens during lactation in the development of atopic disease in childhood.

Sausenthaler (2007) and Willers (2007) have investigated the effect of maternal diet during pregnancy on eczema at 2 years and 5 years respectively. Both observed a statistically significant decreased risk of eczema associated with high maternal fish intake during pregnancy (after adjustment). These findings are supported by Romieu (2007) who also reported a statistically significantly decreased risk of eczema (and wheeze) at one year with high maternal fish intake. No other statistically significant findings are reported.

Willers (2008) was the only study indentified, which reported asthma as an outcome. No consistent associations between maternal intake of investigated food groups during pregnancy and childhood asthma symptoms until 8 years of age were observed, expect for nut products. A decreased risk of wheeze, asthma symptoms and doctor diagnosed asthma is reported when “daily” nut product consumption was compared with “rare” consumption. This association was not found for nuts as such, or when “regular” nut product consumption was compared to “rare” consumption. It
is worth noting that the authors report that the finding is not associated with peanut allergy at 8 years and is independent from the child’s diet.

See table 1 for summary table of study details

**Summary of literature on early life feeding practices and development of atopic disease in childhood.**


**Timing of introduction of any solids and development of atopic outcomes**


Six of these studies report no statistically significant associations between early introduction (before 3 or 4 months) or delayed introduction of solids (after 6 months of age) with eczema. Snijders (2008), however, reports a statistically significant increased risk of eczema, atopic dermatitis and recurrent wheeze with later introduction of solid foods (over the first 12 months of life). Alm (2008) reports no significant associations between timing of introduction of solids foods and eczema.

Two studies investigated the timing of introduction of solid foods and development of asthma in childhood (Mihrshahi (2007) and Zutavern (2007). Neither of these studies reported a statistically significant association.

**Diversity of weaning diet and development of atopic outcomes**

Zutavern (2008) reports a statistically significant increased risk of eczema with a more diverse diet if children who had early signs of eczema had been excluded from the analysis (to limit reverse causality). Filipiak (2007) reports findings from a prospective birth cohort study in which the cohort was divided into an intervention group (high risk infants with infant feeding recommendations) and a non-intervention group (non-high risk infants with no infant feeding recommendations). Filipiak (2007) reports no association between diversity of weaning diet and development of eczema in a high risk group of infants.

**Timing of introduction of allergenic foods and atopic outcomes**

Four studies investigated the effect of timing of introduction of specific allergenic foods and atopic outcomes (Kull (2006), Fussman (2007), Snijders (2008) and Alm (2008). No studies have been identified which have investigated timing of introduction of peanuts or nuts.
Fussman (2007) analysed exposure to milk in the first three years of life and risk of asthma using four modelling techniques (concurrent, delayed, combined and reverse delayed). No statistically significant associations in the concurrent, delayed and combined models were observed. However, a statistically significant decreased risk of asthma at three years associated with milk consumption was reported when the delayed model was stratified by study period. The authors suggest that this finding may be attributed to reverse causation as the reverse causation model shows that asthma presence is statistically significantly negatively associated with exposure to cows’ milk in the next study period. Kull (2006) has reported a decreased risk of asthma and eczema with exposure to fish between 3-8 months versus introduction at 9 months of age or after. This finding is supported by Alm (2008), who report a decreased risk of eczema at one year of age with introduction of fish before the first 9 months of age. Snijders (2008) also investigated the association between timing of introduction of cows’ milk as well as other solid foods. A statistically significant increased risk of eczema was reported with more delay in introduction of cows’ milk over the first 12 months of life. No statistically significant associations, however, were reported for atopic dermatitis or recurrent wheeze.

Timing of introduction of allergenic foods as part of a whole dietary pattern

Four studies presented data on the effect of exposure to allergens in early life as part of a whole dietary pattern (Mihrshahi (2007), Zutavern (2008), Filipiak (2007) and Dunlop (2006). Mihrshahi (2007) and Zutavern (2008) report no statistically significant associations with risk of asthma or eczema and timing of introduction of food allergens. Filipiak (2007) reports no statistically significant associations in the intervention group. In the non-intervention group, however, a statistically significant decreased risk of eczema is reported in the non-intervention group if soy and nuts are introduced after 6 months of age and a statistically significant increased risk of eczema in the non-intervention group if egg was not introduced in the first year of life. Dunlop (2006) investigated exposure to four food allergens (eggs, fish, cows’ milk and nuts) and reported a statistically significant increased risk of atopic dermatitis if eggs and fish are introduced in the first year of life. No statistically significant associations, however, are reported for exposure to cows’ milk or nuts.

See table 2 for summary table of study details

Multi-faceted interventions to reduce the risk of atopic disease in childhood

One study was identified which involved a multi-faceted intervention to reduce the risk of atopic disease in children. This study was conducted in a high risk population which was randomised into two study groups. The intervention group involved three interventions 1.) childhood dietary avoidance (dairy, egg, wheat, nuts, soya during first 12 of life), 2.) maternal avoidance during lactation (allergens as before, with the exception of wheat) and 3.) reduction in house dust mite exposure. The study reports a statistically significantly decreased risk of asthma, allergic asthma, atopic dermatitis and allergic dermatitis to 8 years of age in the intervention group compared with the control group.

See table 3 for study details.
Table 1: Summary of literature on maternal dietary exposure to food allergens and development of atopic disease in childhood.

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<tbody>
<tr>
<td>Study design</td>
<td>Birth cohort study (LISA)(^1)</td>
<td>Birth cohort study</td>
<td>Birth cohort study (PIAMA)(^2)</td>
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</tr>
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<td>Spain</td>
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<td>High risk?</td>
<td>General population</td>
<td>General population</td>
<td>General population</td>
<td>Fish intake during pregnancy</td>
</tr>
<tr>
<td>Exposure</td>
<td>Maternal diet during last 4 weeks of pregnancy</td>
<td>Maternal diet during pregnancy (2-3m from 32wks gestation)</td>
<td>Maternal diet during pregnancy</td>
<td>Fish intake during pregnancy</td>
</tr>
<tr>
<td>Atopic Outcomes</td>
<td>Eczema</td>
<td>Eczema</td>
<td>Wheeze and asthma symptoms</td>
<td>Eczema</td>
</tr>
<tr>
<td>Age at follow-up</td>
<td>2 years</td>
<td>5 years</td>
<td>From 1 to 8 years</td>
<td>1 to 6 years</td>
</tr>
</tbody>
</table>

Findings of interest:
- Only one statistically significant finding relating to exposure to allergenic foods was reported: Decreased risk of eczema associated with high maternal fish consumption: aOR 0.75 (0.57-0.98)\(^1\)
- Only one statistically significant finding relating to exposure to allergenic foods was reported: Decreased risk of eczema associated with maternal fish consumption. Doctor-diagnosed eczema: aOR 0.57 (0.32-1.06)\(^2\)
- Only one statistically significant finding relating to exposure to allergenic foods was reported: Increased risk of wheeze, aOR 1.42 (1.06-1.89) and asthma symptoms, aOR 1.47 (1.08-1.99) when comparing daily versus rare nut product consumption.
- Decreased risk of eczema at 1 year with maternal fish consumption: aOR 0.73 (0.55-0.98)
- Decreased risk of atopic wheeze at 6 years with maternal fish consumption: aOR 0.55 (0.31-0.96)

Findings are presented as adjusted odds ratios (aOR) with 95% confidence intervals.

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\(^1\) LISA: Influences of Lifestyle-related Factors on the Immune System and the Development of Allergies in Childhood study

\(^2\) PIAMA: Prevention and Incidence of Asthma and Mite Allergy
Table 2: Summary of literature on early life feeding practices and development of atopic disease in childhood.

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</thead>
<tbody>
<tr>
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<td>Cohort study</td>
<td>Birth cohort study</td>
<td>Birth cohort</td>
<td>Birth cohort</td>
<td>Birth cohort (KOALA)&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Case-control</td>
<td>Birth cohort</td>
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<td>1326</td>
<td>2558</td>
<td>32</td>
<td>4921</td>
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<tr>
<td>Exposure of interest</td>
<td>Timing of introduction of solid foods</td>
<td>Intervention group given infant feeding guidelines (BF &gt;4m, introduce solids &gt;4m, no allergens in first 12m, introduce 1 food item per week).</td>
<td>Timing of introduction of solids (and allergenic foods)</td>
<td>Timing of introduction of solids (and allergenic foods)</td>
<td>Dietary exposure to cows' milk in first 3 years</td>
<td>Dietary fish exposure</td>
<td>Timing of introduction of solids (and allergenic foods)</td>
<td>Timing of introduction of Cows' milk products and other foods products</td>
<td>Timing of introduction of solids</td>
<td>Dietary exposure/Timing of introduction to solids and food allergens</td>
</tr>
<tr>
<td>Atopic Outcomes</td>
<td>Atopic dermatitis</td>
<td>Eczema Asthma</td>
<td>Eczema Asthma</td>
<td>Asthma</td>
<td>Eczema Asthma</td>
<td>Asthma</td>
<td>Atopic Eczema</td>
<td>Eczema Asthma</td>
<td>Eczema Asthma</td>
<td>Eczema</td>
</tr>
</tbody>
</table>

<sup>3</sup> GINI: German Infant Nutritional Intervention program  
<sup>4</sup> KOALA: Child, Parent and Health: lifestyle and genetic constitution
### Details of Study

<table>
<thead>
<tr>
<th>Study</th>
<th>Age at follow-up</th>
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<tr>
<td>Sahakyan, 2006</td>
<td>To 7 years</td>
</tr>
<tr>
<td>Filipiak, 2007</td>
<td>4 years</td>
</tr>
<tr>
<td>Mihrshahi, 2007</td>
<td>5 years</td>
</tr>
<tr>
<td>Zutavern, 2008</td>
<td>6 years</td>
</tr>
<tr>
<td>Fussman, 2007</td>
<td>3 years</td>
</tr>
<tr>
<td>Kull, 2006</td>
<td>4 years</td>
</tr>
<tr>
<td>Dunlop, 2006</td>
<td>1 year</td>
</tr>
<tr>
<td>Snijders, 2008</td>
<td>2 years</td>
</tr>
<tr>
<td>Estrada-Reyes, 2007</td>
<td>3 years</td>
</tr>
<tr>
<td>Alm, 2008</td>
<td>1 year</td>
</tr>
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</table>

### Findings of interest

<table>
<thead>
<tr>
<th>Study</th>
<th>Findings of interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sahakyan, 2006</td>
<td>No statistically significant associations with timing of introduction of solids (&lt;4m or &gt;6m) and atopic dermatitis to 7 years</td>
</tr>
<tr>
<td>Filipiak, 2007</td>
<td>Intervention group: No statistically significant associations between timing or diversity of solids with eczema. Control group: reduced risk of eczema if soy and nuts introduced &gt;6m and increased risk if eggs not introduced &lt;12m</td>
</tr>
<tr>
<td>Mihrshahi, 2007</td>
<td>No statistically significant associations between early solid feeding (by 3m) and introduction of food allergens by 9m</td>
</tr>
<tr>
<td>Zutavern, 2008</td>
<td>No statistically significant associations with introduction of solids &gt;4m or 6m and asthma, introduction of solids (&gt;4/6m) or diversity of diet and eczema in whole cohort. If children with early symptoms of eczema are removed, risk of eczema is increased in children who received a more diverse diet at 4m (aOR 2.72 (1.24-5.99))</td>
</tr>
<tr>
<td>Fussman, 2007</td>
<td>No statistically significant associations with cows’ milk exposure using unstratified data in concurrent, delayed and combined models and asthma. If data is stratified by study period the cows’ milk exposure statistically significantly decreases the risk of asthma: aOR 0.56 (0.34-0.87) and 0.57 (0.43-0.76)</td>
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<tr>
<td>Kull, 2006</td>
<td>Fish consumption between 3 and 8m versus &gt;9m is associated with a statistically significant decreased risk of asthma and eczema. aOR 0.55 (0.34-0.87) and 0.57 (0.43-0.76)</td>
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<tr>
<td>Dunlop, 2006</td>
<td>No statistically significant associations between introduction of solids &lt;4m and atopic eczema. Exposure to eggs and fish in the first year of life was associated with increased risk of atopic eczema. aOR 1.92 (1.2-3.2) and 1.56 (1.1-2.3). No associations were reported for cows’ milk and nut consumption.</td>
</tr>
<tr>
<td>Snijders, 2008</td>
<td>Increased risk of eczema with later introduction of cows’ milk-0.3m versus &gt;9m: aOR 2.29 (1.21-4.33)</td>
</tr>
<tr>
<td>Estrada-Reyes, 2007</td>
<td>Increased risk of eczema, atopic dermatitis and wheeze with later introduction of other food products: aOR 2.10 (1.17-3.76), 9.46 (2.05-43.61) and 3.52 (1.42-8.73)</td>
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<tr>
<td>Alm, 2008</td>
<td>A statistically significant decreased risk in eczema at one year with introduction of fish &lt;9m OR0.76 (0.62-0.94)</td>
</tr>
</tbody>
</table>

*aOR= adjusted odds ratio. Findings are presented as odds ratios with 95% confidence intervals.

* Significance level set to P< 0.01 in Alm (2008)
Table 3: Summary of literature on multi-faceted interventions to reduce risk of atopic disease in childhood

<table>
<thead>
<tr>
<th>Details of Study</th>
<th>Arshad, 2007</th>
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<tr>
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<tr>
<td>High risk?</td>
<td>High risk population</td>
</tr>
<tr>
<td>Exposure</td>
<td>Combination of three interventions 1.) childhood dietary avoidance (dairy, egg, wheat, nuts, soya during first 12 of life), 2.) maternal avoidance during lactation (allergens as before, with the exception of wheat) and 3.) reduction in house dust mite exposure.</td>
</tr>
<tr>
<td>Atopic Outcomes</td>
<td>Asthma</td>
</tr>
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<td></td>
<td>Atopic dermatitis</td>
</tr>
<tr>
<td>Age at follow-up</td>
<td>1 to 8 years</td>
</tr>
<tr>
<td>Findings of interest</td>
<td>Intervention group had a statistically significantly decreased risk of asthma and atopic dermatitis compared with the control group: aOR 0.24 (0.09-0.66) and aOR 0.23 (0.08-0.64)</td>
</tr>
</tbody>
</table>

Findings are presented as adjusted odds ratios (aOR) with 95% confidence intervals.
Included references

Literature on maternal dietary exposure to food allergens and development of atopic disease in childhood

Sausenthaler, 2007
Maternal diet during pregnancy in relation to eczema and allergic sensitisation.
*American Journal of Clinical Nutrition.* **85** 530-7

Willers, 2007
Maternal consumption during pregnancy and asthma, respiratory and atopic symptoms in 5 year olds.
*Thorax** **62** 773-779

Willers, 2008
Maternal food consumption during pregnancy and the longitudinal development of childhood asthma.
*American Journal of Respiratory and Critical Care Medicine* **178** 124-131

Romieu, 2007
Maternal fish intake during pregnancy and atopy and asthma in infancy.
*Clinical and Experimental Allergy* **37** 518-525

Literature on early life feeding practices and development of atopic disease in childhood.

Sahakyan, 2006
Feeding patterns of babies and the development of atopic dermatitis in children after 12 months of age in Armenia: is there a signal?
*European Journal of Epidemiology* **21** 723-725

Filipiak, 2007
Solid food introduction in relation to eczema: results from a four-year prospective birth cohort study.
*Journal of Pediatrics* **151** 352-358

Mahrshahi, 2007
The association between infant feeding practices and subsequent atopy among children with a family history of asthma.
*Clinical and Experimental Allergy* **37** 671-679

Zutavern, 2008
Timing of solid food introduction in relation to eczema, asthma, allergic rhinitis, and food and inhalant sensitisation at the age of 6 years: results from the prospective birth cohort study LISA.
*Pediatrics* **121** e44-52

Fussman, 2007
Cows’ milk exposure and asthma in a newborn cohort: repeated ascertainment indicates reverse causality.
Journal of Asthma 44 99-105

Kull, 2006
Fish consumption during the first year of life and the development of allergic diseases during childhood.
Allergy 61 1009-1015

Dunlop, 2006
Environmental and dietary risk factors for infantile atopic eczema and Slovak birth cohort.
Pediatric Allergy and Immunology 17 103-111

Snijders, 2008
Age at first introduction of cow milk products and other food products in relation to infant atopic manifestation in the first 2 years of life: the KOALA birth cohort study.
Pediatrics 122 e115-122

Estrada-Reyes, 2007
A case-control study of food hypersensitivity, timing of weaning and family history of allergies in young children with atopic dermatitis.
Allergology and Immunopathology 35 101-4

Alm, 2008
Early introduction of fish decreases the risk of eczema in infants.
Archives of Diseases in Childhood. DOI: 10.1136/adc.2008.140418

Literature on multi-faceted interventions to reduce risk of atopic disease in childhood

Arshad, 2007
Prevention of allergic disease during childhood by allergen avoidance: The Isle of Wight prevention study.
Journal of Allergy and Clinical Immunology 119 307-313
2.3: Full text papers summarised in section 2.1

1.) Maternal dietary antigen avoidance during pregnancy or lactation, or both, for preventing or treating atopic disease in the child (Review). Kramer, MS. Kakuma, R. (2006) Cochrane Database of Systematic Reviews. 3 Art. No.: CD000133. DOI:10.1002/14651858.CD000133.pub2

http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD000133/frame.html


http://pediatrics.aappublications.org/cgi/reprint/121/1/183


http://download.journals.elsevierhealth.com/pdfs/journals/0091-6749/PiIS009167490800955X.pdf


2.4: Abstracts of fifteen papers summarised in section 2.2
2.4 Abstracts for literature on food allergen exposure in early life and development of atopic disease

Literature on maternal dietary exposure to food allergens and development of atopic disease in childhood

<table>
<thead>
<tr>
<th>Title</th>
<th>Maternal diet during pregnancy in relation to eczema and allergic sensitization in the offspring at 2 y of age.</th>
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</table>

**Abstract**

**BACKGROUND:** Maternal diet during pregnancy might be one of the factors that influences fetal immune responses associated with childhood allergy. 

**OBJECTIVE:** We analyzed the association between maternal diet during the last 4 wk of pregnancy and allergic sensitization and eczema in the offspring at 2 y of age. 

**DESIGN:** Data from 2641 children at 2 y of age were analyzed within a German prospective birth cohort study (LISA). Maternal diet during the last 4 wk of pregnancy was assessed with a semiquantitative food-frequency questionnaire, which was administered shortly after childbirth. 

**RESULTS:** High maternal intake of margarine [adjusted odds ratio (aOR): 1.49; 95% CI: 1.08, 2.04] and vegetable oils (aOR: 1.48; 95% CI: 1.14, 1.91) during the last 4 wk of pregnancy was positively associated and high maternal fish intake (aOR: 0.75; 95% CI: 0.57, 0.98) was inversely associated with eczema during the first 2 y in the offspring. High celery (aOR: 1.85; 95% CI: 1.18, 2.89) and citrus fruit (aOR: 1.73; 95% CI: 1.18, 2.53) increases the risk of sensitization against food allergens. In turn, sensitization against inhalant allergens was positively related to a high maternal intake of deep-frying vegetable fat (aOR: 1.61; 95% CI: 1.02, 2.54), raw sweet pepper (aOR: 2.16; 95% CI: 1.20, 3.90), and citrus fruit (aOR: 1.72; 95% CI: 1.02, 2.92). 

**CONCLUSIONS:** We suggest that the intake of allergenic foods and foods rich in n-6 polyunsaturated fatty acids during pregnancy may increase and foods rich in n-3 polyunsaturated fatty acids may decrease the risk of allergic diseases in the offspring.

<table>
<thead>
<tr>
<th>Title</th>
<th>Maternal food consumption during pregnancy and asthma, respiratory and atopic symptoms in 5-year-old children</th>
</tr>
</thead>
</table>

**Abstract**

**BACKGROUND:** Associations between maternal vitamin E, vitamin D and zinc intakes during pregnancy and asthma, wheeze and eczema in 5-year-old children have previously been reported. A study was undertaken to investigate whether maternal intake of specific foods during pregnancy is associated with asthma and allergic outcomes in the same children. 

**METHODS:** A longitudinal birth cohort study was conducted in 1,924 children born to women recruited during pregnancy. Maternal diet during pregnancy was assessed by food frequency questionnaire (FFQ). Cohort children were followed up at 5 years by symptom questionnaire and FFQ. Food groups of interest were fruit, vegetables, fruit juice, whole grain products, fish, dairy products and fat spreads. Trends across outcome groups defined by level of food intake are presented. 

**RESULTS:** 1,253 children participated at 5 years and maternal FFQ data were available for 1,212. No consistent associations were found between childhood outcomes and maternal intake of the analysed foods except for apples and fish. Maternal apple intake was beneficially associated with ever wheeze (OR highest vs lowest tertile 0.63, 95% CI 0.42 to 0.95), ever asthma (OR 0.54, 95% CI 0.32 to 0.92) and doctor-confirmed asthma (OR 0.47, 95% CI 0.27 to 0.82) in the children. Maternal fish consumption was beneficially associated with doctor-
confirmed eczema (OR >or=1/week vs never 0.57, 95% CI 0.35 to 0.92).

CONCLUSION: There was no evidence for associations between maternal intake of most foods during pregnancy and asthma, respiratory and allergic outcomes in 5-year-old children, except for apples and fish. Consumption of apples and fish during pregnancy may have a protective effect against the development of childhood asthma and allergic disease.

Title: Maternal consumption during pregnancy and the longitudinal development of childhood asthma

Authors: Willers, SM. Wijga, A. Bruneckreef, B. Kerkhof, M. Gerritsen, J. Hoekstra, M. de Jongste, J. Smit, H.


Abstract

RATIONALE: Maternal diet during pregnancy has the potential to affect airway development and to promote T-helper-2–cell responses during fetal life. This might increase the risk of developing childhood asthma or allergy.

Objectives: We investigated the influence of maternal food consumption during pregnancy on childhood asthma outcomes from 1 to 8 years of age.

METHODS: A birth cohort study consisting of a baseline of 4,146 pregnant women (1,327 atopic and 2,819 nonatopic). These women were asked about their frequency of consumption of fruit, vegetables, fish, egg, milk, milk products, nuts, and nut products during the last month. Their children were followed until 8 years of age. Longitudinal analyses were conducted to assess associations between maternal diet during pregnancy and childhood asthma outcomes over 8 years.

MEASUREMENTS AND MAIN RESULTS: Complete data were obtained for 2,832 children. There were no associations between maternal vegetable, fish, egg, milk or milk products, and nut consumption and longitudinal childhood outcomes. Daily consumption of nut products increased the risk of childhood wheeze (odds ratio [OR] daily versus rare consumption, 1.42; 95% confidence interval [95% CI], 1.06–1.89), dyspnea (OR, 1.58; 95% CI, 1.16–2.15), steroid use (OR, 1.62; 95% CI, 1.06–2.46), and asthma symptoms (OR, 1.47; 95% CI, 1.08–1.99).

CONCLUSION: Results of this study indicate an increased risk of daily versus rare consumption of nut products during pregnancy on childhood asthma outcomes. These findings need to be replicated by other studies before dietary advice can be given to pregnant women.

Title: Maternal fish intake during pregnancy and atopy and asthma in infancy

Authors: Romieu, I.Torrent, M.Garcia-Esteban, R. Ferrer, C. Ribas-Fitó , N. Antó, M. Sunyer , J.

Reference: Clinical and Experimental Allergy. 37 (4) 518-525 2007

Abstract

BACKGROUND: There is growing evidence that n-3 fatty acids have anti-inflammatory properties and may modulate immune response. Dietary intake of these nutrients during pregnancy could play a role in the risk of asthma and atopy in the offspring.

METHODS: Using data from a cohort of women (n=462) enrolled during pregnancy and whose offspring were followed up to 6 years, we evaluated the impact of fish consumption during pregnancy on the incidence of atopy and asthma. Dietary intake was assessed by food frequency questionnaire (42 items) applied by an interviewer.

RESULTS: Thirty-four percent of infants had a medical diagnosis of eczema at age 1 year, 14.3% of the children were atopic [based on skin prick test (SPT) at 6 years], and 5.7% had atopic wheeze at age 6 years. After adjusting for potential confounding factors, fish intake during pregnancy was protective against the risk of eczema at age 1 year, a positive SPT for house dust mite at age 6 years and atopic wheeze at age 6 years [odds ratio (OR)=0.73 95% confidence interval (CI) 0.55–0.98, OR=0.68, 95% CI 0.46–1.01 and OR=0.55, 95% CI 0.31–0.96, respectively]. For an increase in fish intake from once per
week to 2.5 times per week, the risk of eczema at age 1 year decreased by 37%, and the risk of positive SPT at age 6 years by 35%. Stratification by breastfeeding showed that fish intake was significantly related to a decrease risk in persistent wheeze among non-breastfed children ($P$ for interaction <0.05). No protective effect was observed among breastfed children.

CONCLUSION: Our data suggest a protective effect of fish during pregnancy on the risk of atopy-related outcomes.

Literature on early life feeding practices and development of atopic diseases in childhood

<table>
<thead>
<tr>
<th>Title</th>
<th>Feeding practices of babies and the development of atopic dermatitis in children after 12 months of age in Armenia: is there a signal?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Authors</td>
<td>Sahakyan A.  Armenian HK.  Breitscheidel L.  Thompson ME.  Enokyan G.</td>
</tr>
<tr>
<td>Abstract</td>
<td>We investigated the influence of feeding practices on development of atopic dermatitis (AD) in Armenian children (n = 240). In multivariate models early introduction to solids, family history of atopy, and breastfeeding by a mother with atopic condition were associated with the development of AD after 12 months post-term. A prospective study in Armenia is recommended to confirm our findings.</td>
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<table>
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<tr>
<th>Title</th>
<th>Solid food introduction in relation to eczema: results from a four-year prospective birth cohort study.</th>
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<tr>
<td>Abstract</td>
<td>OBJECTIVE: To assess the association between the introduction of solid foods in the first 12 months and the occurrence of eczema during the first 4 years of life in a prospective study of newborns. STUDY DESIGN: Data were taken from annually administered questionnaires from a large birth cohort (recruited 1995-1998) comprised of an intervention and a nonintervention group. Outcomes were doctor-diagnosed and symptomatic eczema. Multiple generalized estimation equation models were performed for the 2 study groups. RESULTS: From the 5991 recruited infants, 4753 (79%) were followed up. The 2 study groups were different in their family risk of allergies and feeding practices. No association was found between the time of introduction of solids or the diversity of solids and eczema. In the nonintervention group, a decreased risk was observed for avoidance of soybean/nuts, but an increased risk was seen in doctor-diagnosed eczema for the avoidance of egg in the first year. CONCLUSION: The evidence from this study supports neither a delayed introduction of solids beyond the fourth month nor a delayed introduction of the most potentially allergenic solids beyond the sixth month of life for the prevention of eczema. However, effects under more extreme conditions cannot be ruled out.</td>
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<tr>
<th>Title</th>
<th>The association between infant feeding practices and subsequent atopy among children with a family history of asthma.</th>
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<tbody>
<tr>
<td>Authors</td>
<td>Mihrshahi S.  Amporn R.  Webb K.  Almqvist C.  Kemp AS.  Hector D.  Marks GB.  CAPS Team.</td>
</tr>
<tr>
<td>Reference</td>
<td>Clinical &amp; Experimental Allergy. 37(5):671-9, 2007 May.</td>
</tr>
</tbody>
</table>
| Abstract | BACKGROUND: Although longer duration of breastfeeding and later introduction of solid foods are both recommended for the prevention of asthma and allergic disease, evidence to support these recommendations is controversial. OBJECTIVE: To examine the relation between infant feeding practices and the
risk of asthma and allergic disease at age 5 years.

METHODS: A cohort of children with a family history of asthma in Sydney, Australia, was followed from birth to age 5 years. Data on infant feeding practices and on early manifestations of eczema were collected prospectively. The presence of eczema, asthma and atopy (positive allergen skin prick tests) were determined at age 5 years.

RESULTS: In 516 children evaluated at age 5 years, there was no significant association between the duration of breastfeeding or timing of introduction of solid foods and protection against asthma or other allergic disease, after adjustment for confounding factors. However, breastfeeding for 6 months or more and introduction of solid foods after 3 months were both associated with an increased risk of atopy at age 5 years (P=0.02 and 0.01, respectively). There was no significant association between the presence of eczema at 4 weeks and at 3 months and continued breastfeeding beyond those times.

CONCLUSION: Longer duration of breastfeeding and later introduction of solid foods did not prevent the onset of asthma, eczema or atopy by age 5 years.

Title Timing of solid food introduction in relation to eczema, asthma, allergic rhinitis, and food and inhalant sensitization at the age of 6 years: results from the prospective birth cohort study LISA.


Abstract OBJECTIVE: Current prophylactic feeding guidelines recommend a delayed introduction of solids for the prevention of atopic diseases. This study investigates whether a delayed introduction of solids (past 4 or 6 months) is protective against the development of eczema, asthma, allergic rhinitis, and food or inhalant sensitization at the age of 6 years.

METHODS: Data from 2073 children in the ongoing LISA birth cohort study were analyzed at 6 years of age. Multivariate logistic regression analyses were performed for all children and for children without skin or allergic symptoms within the first 6 months of life to take into account reverse causality.

RESULTS: A delayed introduction of solids (past 4 or 6 months) was not associated with decreased odds for asthma, allergic rhinitis, or sensitization against food or inhalant allergens at 6 years of age. On the contrary, food sensitization was more frequent in children who were introduced to solids later. The relationship between the timing of solid food introduction and eczema was not clear. There was no protective effect of a late introduction of solids or a less diverse diet within the first 4 months of life. However, in children without early skin or allergic symptoms were considered, eczema was significantly more frequent in children who received a more diverse diet within the first 4 months.

CONCLUSIONS: This study found no evidence supporting a delayed introduction of solids beyond 4 or 6 months for the prevention of asthma, allergic rhinitis, and food or inhalant sensitization at the age of 6 years. For eczema, the results were conflicting, and a protective effect of a delayed introduction of solids cannot be excluded. Positive associations between late introduction of solids and food sensitization have to be interpreted with caution. A true protective effect of a delayed introduction of solids on food sensitization seems unlikely.

Title Cow's milk exposure and asthma in a newborn cohort: repeated ascertainment indicates reverse causation.

Authors Fussman C. Todem D. Forster J. Arshad H. Urbanek R. Karmaus W.


Abstract The effect of cow's milk consumption on childhood asthma has been debated for several years. This study attempts to provide further insight into this association through the use of a longitudinal study design. Newborns from parents with atopic history were recruited from Germany, Austria, and England (n = 696). For five repeated ascertainment, information was collected on cow's milk exposure,
incidence of doctor-diagnosed asthma, and confounders. Generalized estimation equations, incorporating different models (concurrent, delayed, combined, and reverse causation), were used to determine this association. No association between cow's milk consumption and childhood asthma was found for the concurrent effects model (OR = 0.81, 95% confidence interval [CI]: 0.55, 1.20). In the delayed effects model, the direction of the association varied with time of follow-up. Thus, we stratified by period, which resulted in a significant protective delayed effect at 36 months (OR = 0.18, 95% CI = 0.06, 0.49). However, reverse causation negated this finding since the presence of asthma in prior months led to a reduction in further exposure to cow's milk (OR = 0.40, 95% CI = 0.16, 0.99). Hence, cow's milk consumption does not protect against childhood asthma. The apparent protection of cow's milk against asthma may result from parents of asthmatic children avoiding cow's milk, rather than actual prophylaxis.

### Abstract

**Fish consumption during the first year of life and development of allergic diseases during childhood.**

**Authors** Kull I., Bergström A., Lilja G., Pershagen G., Wickman M.


**Abstract**

BACKGROUND: Fish consumption during infancy has been regarded as a risk factor for allergic disease but later evidence suggests a protective role. However, methodological limitations in the studies make conclusions uncertain. The aim of this study was to assess the association between fish consumption during the first year of life and development of allergic diseases by age 4.

METHODS: A prospective birth cohort of 4089 new-born infants was followed for 4 years using parental questionnaires at ages 2 months, 1, 2 and 4 years to collect information on exposure and health effects. The response rate at 4 years was 90%. A clinical investigation was performed at age 4 years, which included blood sampling for analysis of specific IgE to common food and airborne allergens.

RESULTS: Parental allergic disease and onset of eczema or wheeze during the first year of life delayed introduction of fish in the child's diet. After exclusion of such children to avoid disease-related modification of exposure, regular fish consumption during the first year of life was associated with a reduced risk for allergic disease by age 4, OR(adj) 0.76 (95% CI 0.61-0.94) and sensitization, OR(adj) 0.76 (0.58-1.0). The reduced risk appeared most pronounced for multiple disease, OR(adj) 0.56 (0.35-0.89). IgE-sensitization to fish was only present among 18 of the 2614 children.

CONCLUSION: Regular fish consumption before age 1 appears to be associated with a reduced risk of allergic disease and sensitization to food and inhalant allergens during the first 4 years of life.

### Abstract

**Environmental and dietary risk factors for infantile atopic eczema among a Slovak birth cohort.**

**Authors** Dunlop AL., Reichrtova E., Palcovicova L., Ciznar P., Adamcakova-Dodd A., Smith SJ., McNabb SJ.

**Reference** Pediatric Allergy & Immunology. 17(2):103-11, 2006 Mar.

**Abstract** Infantile atopic eczema (AE) is a risk marker for future asthma. This study assesses the contribution of modifiable exposures to infantile AE. If modifiable exposures contribute substantially to infantile AE, its prevention might be a sensible approach to asthma prevention. Pregnant women (n = 1978) were systematically recruited from maternity hospitals of the Slovak Republic; their birthed cohort of 1990 children were prospectively followed for 1 yr. Children's exposures to selected environmental and dietary factors were assessed via maternal questionnaires administered at delivery and 1 yr of age. A child was considered to have AE, based on physical examination (SCORAD index >2) or mother's report of a previous physician diagnosis. Multivariate logistic regression was used to calculate adjusted odds ratios and percent total regression scores (TRS) for each variable. At 1 yr of age 1326 (67%) of the
children remained in the cohort and 207 (15.6%) developed AE. Various modifiable environmental and dietary exposures increased the likelihood of AE (ownership of cats; consumption of infant formula, eggs, and fish) while others decreased the likelihood of AE (ownership of livestock; exclusive breast feeding for > or =4 months). Overall, modifiable exposures contributed less to the TRS than did non-modifiable exposures (38% vs. 62%, respectively). The modifiable exposure category that contributed most to the TRS was infant feeding practices (27.5% TRS). Modifiable exposures -- especially those related to infant feeding practices -- significantly contribute to infantile AE, although modifiable factors contribute less overall than do non-modifiable exposures.

<table>
<thead>
<tr>
<th>Title</th>
<th>Age at first introduction of cow milk products and other food products in relation to infant atopic manifestations in the first 2 years of life: the KOALA Birth Cohort Study.</th>
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<tbody>
<tr>
<td>Authors</td>
<td>Snijders BE. Thijs C. van Ree R. van den Brandt PA.</td>
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</tbody>
</table>

**Abstract**

OBJECTIVES: Scientific evidence is scarce about timing of solid-food introduction and its association with the development of atopy. We aimed to evaluate any associations between the introduction of cow milk products/other solid food products and infant atopic manifestations in the second year of life, taking into account reverse causation.

METHODS: Data from 2558 infants in an ongoing prospective birth cohort study in the Netherlands were analyzed. Data on the main determinants (introduction of cow milk products and other food products), outcomes (eczema; atopic dermatitis [United Kingdom Working Party criteria]; recurrent wheeze; any sensitization; sensitization against cow milk, hen egg, peanut, and at least 1 inhalant allergen), and confounders were collected by repeated questionnaires at 34 weeks of gestation and 3, 7, 12, and 24 months postpartum. Information on sensitization was gathered by venous blood collections performed during home visits at age 2. Analyses were performed by multiple logistic regression analyses.

RESULTS: More delay in introduction of cow milk products was associated with a higher risk for eczema. In addition, a delayed introduction of other food products was associated with an increased risk for atopy development at the age of 2 years. Exclusion of infants with early symptoms of eczema and recurrent wheeze (to avoid reverse causation) did not essentially change our results.

DISCUSSION: Delaying the introduction of cow milk or other food products may not be favorable in preventing the development of atopy.

<table>
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<th>Title</th>
<th>A case-control study of food hyper-sensitivity, timing of weaning and family history of allergies in young children with atopic dermatitis.</th>
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<tbody>
<tr>
<td>Authors</td>
<td>Estrada-Reyes E. Pardo-Castaneda MG. Toledo-Bahena ME. Lerma-Ortiz ML. del Rio-Navarro B. Nava-Ocampo AA.</td>
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</table>

**Abstract**

BACKGROUND: The aim of this study was to investigate the relationship between food hypersensitivity and atopic dermatitis (AD) in young children. MATERIAL AND METHODS: In a case-control design, 28 patients < 3 years old, with AD and 28 age-matched healthy children were included in the study. A detailed medical history of allergies and timing of weaning was obtained. Children underwent skin tests (prick and patch) to evaluate food hypersensitivity. The status of DA and food allergies in the study participants was investigated 4 years later.

RESULTS: There were more children with positive skin tests for food hypersensitivity among cases than controls, OR 4.2 (95%CI 1.3 to 13.4). In contrast, there were no differences in the number of children with positive family history of allergic diseases or weaned at < or = 6 months of age between
groups. Four years later, out of the 28 original cases, the state of AD was investigated in 13 (46.4%) infants. Of them, 11 followed an exclusion diet; 6 (46.1%) remained with AD. Of 28 original controls, 15 (51.7%) infants were investigated 4 years later; only one case developed AD.

CONCLUSIONS: Young children who had hypersensitivity to cow’s milk, hen egg, wheat, fish, soy, or legumes were found to have a higher risk of AD. Positive family history of allergies and early weaning were not found to be relevant risk factors.

<table>
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<tr>
<th>Title</th>
<th>Early introduction of fish decreases the risk of eczema in infants</th>
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<tr>
<td>Authors</td>
<td>Alm B. Aberg N. Erdes L. Mollborg P. Petterson R. Norvenius G. Goksor E. Wennergren G.</td>
</tr>
<tr>
<td>Reference</td>
<td>Archives of Diseases in Childhood. DOI: 10.1136/adc.2008.140418 2008</td>
</tr>
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</table>

BACKGROUND: The prevalence of eczema in infants has increased in western societies. It has been suggested that environmental factors and the introduction of food affect the risk of eczema.

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

METHODS: Data were obtained from a prospective, longitudinal study of a cohort of infants born in the region of western Sweden in 2003; 8176 families (50% of the birth cohort) were randomly selected and, at six months of age, they received an invitation to participate, together with a questionnaire. The families that agreed received another questionnaire when the infants were twelve months old. Answers to both questionnaires and Medical birth register data were obtained for 4921 infants, i.e. 60.2% of the originally selected population.

RESULTS: At one year of age, 20.9% of the infants had previous or current eczema. The median age at onset was four months. In the multivariable analysis, a familial occurrence of eczema, especially in siblings (OR 1.87; 95% confidence interval 1.50-2.33) or the mother (OR 1.4; 95% CI 1.30-1.84), remained as an independent risk factor. Beneficial effects of introducing fish before nine months of age (OR 0.76; 95% CI 0.62-0.94) and having a bird in the home (OR 0.35; 95% CI 0.17-0.75) were seen. We found no effects from short-term breast-feeding, the age at which milk or eggs were introduced, a cat or dog in the home or parental smoking.

CONCLUSIONS: One in five infants suffer from eczema during its first year of life. A familial occurrence of eczema increased the risk. Beneficial effects were seen from introducing fish before nine months of age or having a bird in the home. The duration of breast-feeding or the age at which milk or eggs were introduced did not affect the risk of eczema.

Literature on Multi-faceted Interventions

<table>
<thead>
<tr>
<th>Title</th>
<th>Prevention of allergic disease during childhood by allergen avoidance: the Isle of Wight prevention study</th>
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<tr>
<td>Authors</td>
<td>Arshad SH. Bateman B. Sadeghnejad A. Gant C. Matthews SM.</td>
</tr>
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BACKGROUND: Early life allergen exposure may increase the risk of childhood allergy, but the protective effect of reduction in allergen exposure remains uncertain.

OBJECTIVE: To evaluate the effect of reduction in food and house dust mite (HDM) allergen exposure in infancy in preventing asthma and allergy.

METHODS: Infants, at higher risk because of family predisposition, were recruited prenatally and randomized to prophylactic (n = 58) and control (n = 62) groups. Prophylactic group infants were either breast-fed with mother on a low allergen diet or given an extensively hydrolyzed formula. Exposure to HDM was reduced by the use of an acaricide and mattress covers. The control group followed standard advice. Development of allergic diseases and sensitization to common allergens (atopy) was assessed blindly at ages 1, 2, 4, and 8 years in
all 120 children.

RESULTS: Repeated measurement analysis, adjusted for all relevant confounding variables, confirmed a preventive effect on asthma: adjusted odds ratio (OR), 0.24; 95% CI, 0.09-0.66; P = .005; atopic dermatitis, OR, 0.23; CI, 0.08-0.64; P = .005; rhinitis, OR, 0.42; CI, 0.19-0.92; P = .03; and atopy, OR, 0.13; CI, 0.05-0.32; P < .001. The protective effect was primarily observed in the subgroup of children with persistent disease (symptoms at all visits) and in those with evidence of allergic sensitization. CONCLUSION: Allergic diseases can be reduced, for at least the first 8 years of life, by combined food and HDM allergen avoidance in infancy.

CLINICAL IMPLICATIONS: Strict food and HDM allergen avoidance should be considered for prevention of allergy in high-risk infants.