Science-Based Evidence on Allergy Prevention in Infancy and Childhood

Prevention of Atopic Eczema by Nutritional Intervention during Infancy
Sibylle Koletzko, Munich (Germany)

Nutrition Strategies to Prevent Food Allergy
Debra J. Palmer, Crawley, W.A. (Australia)

The Health and Economic Impacts of Early Prevention of Atopic Dermatitis
Jörg Spieldenner, Lausanne (Switzerland)
Prevention of Atopic Eczema by Nutritional Intervention during Infancy

Sibylle Koletzko

Division of Pediatric Gastroenterology
Dr. von Hauner Children’s Hospital
Ludwig Maximilians-University, Munich, Germany
sibylle.koletzko@med.uni-muenchen.de

Key Messages
Atopic eczema affects 1 of 3 children with a family history of eczema, with about half of them developing the skin lesions during infancy.

The risk for eczema can be significantly reduced by feeding a hydrolyzed infant formula during the first 4 months of life if breast-feeding is not sufficient.

Atopic eczema is the most common allergic manifestation in the first decade of life with an increasing incidence worldwide. Particularly moderate to severe forms have a major impact on the quality of life of the children and their families (fig. 1). In more than 50% of affected children, atopic eczema develops in infancy. The risk is twice as high in children with a family history of allergy compared to those without any known genetic factors. This holds true for infants who have been exclusively breast-fed for the first 4 months of life and those who received formula. Since it has been recognized that early contact with food allergens plays a role in the development of both tolerance of and sensitization to food antigens, nutritional intervention strategies have been suggested for primary allergy prevention.

Most of these nutritional intervention trials of allergy prevention have been performed in infants with an increased familial risk for allergies. By far the largest trial, the German Infant Nutritional Intervention (GINI) study, included 5,991 children. A non-interventional arm (n = 3,739) followed infants received one of the study formulas, which were packed in identical tins for blinding. There were two ‘normal’ tasting formulas, a standard cow’s milk formula (CMF) and a partially hydrolyzed whey (pHF-W) as well as two bitter tasting extensively hydrolyzed formulas based on either whey (eHF-W) or casein (eHF-C) [1–3]. The children were assessed on a regular basis by questionnaires, physical examinations and blood testing. After 10 years of follow-up, the protective effect of the hydrolyzed formulas on atopic eczema was still evident [4]. Compared with CMF, the hydrolyzed formulas reduced atopic dermatitis, both in the per-protocol analysis and the intention-to-treat analysis including all randomized children except for those who were exclusively breast-fed during the first 6 months of life. These effects were significant for the pHF-W and the eHF-C, while for the eHF-W the results showed borderline effects (fig. 2). The preventive effect of early nutritional intervention developed during infancy and persisted until 10 years of age. During the 10-year follow-up, no significant effect was observed on asthma or allergic rhinitis.

In conclusion, the 10-year follow-up data of the GINI study support the use of hydrolyzed formulas in high-risk infants during the first 4 months of life if exclusive breast-feeding is not possible in order to reduce the burden of eczema in these children.

References
The incidence of food allergy, especially in the first few years of life, has recently increased dramatically. In Australia, pre-schoolers have experienced a 5-fold increase in food anaphylaxis [1], with over 10% of 1-year-olds now having clinical food allergy [2]. Early or late exposure to food allergens in infancy has been identified as a possible food allergy prevention strategy. In 2000, it was recommended that in infants at higher risk of allergy (based on family history), the introduction of allergenic foods be delayed, including avoidance of eggs until 2 years and nuts until 3 years of age [3]. In contrast, over the past decade, recent observational studies have found that a delayed introduction of some foods beyond 6–10 months of age has been associated with an increased risk of allergic diseases. In particular, one cohort study [4] found that delaying the introduction of egg until 10–12 months of age (adjusted OR 1.6, 95% CI 1.0–2.6) was associated with a higher risk of egg allergy compared with an earlier introduction at 4–6 months. In response to these new observations, there has been a major shift in approach, with expert committees worldwide withdrawing their previous recommendations to delay the introduction of allergenic foods [5–8]. However, it is recognised that evidence from randomised controlled trials (RCTs) is needed to determine whether early exposure to food allergens reduces the risk of food allergy.

An RCT investigating the timing of egg exposure in infants with eczema, who tend to have a higher chance of developing food allergies, has now been published [9]. One group of infants (n = 49) was introduced to whole egg powder and the other group of infants (n = 37) was introduced to rice powder from 4 months of age (fig. 1). The families mixed 1 teaspoon of powder with their infant’s solid foods each day until 8 months of age, when cooked egg was introduced to both groups of infants. At 12 months of age, a medically observed egg challenge determined which infants had developed an egg allergy. Overall, 33% of infants introduced to egg from 4 months of age developed an egg allergy compared to 51% of infants introduced to egg from 8 months of age. Unfortunately, the results of this trial did not reach statistical significance due to the trial’s small sample size. Research is continuing with at least 7 current RCTs worldwide investigating whether early food allergen exposure during infancy can prevent food allergy.

Key Messages
Caution needs to be taken when infants with eczema first eat egg or egg-containing foods.

Recent research suggests that a reduction in egg allergy incidence may be achieved by early regular oral egg exposure in infants with eczema, provided that the infants had tolerated their first few exposures to egg.

Caution needs to be taken when infants with eczema first ingest egg in solid foods.

All infants were introduced to cooked egg in their diet.

Intervention from 4 to 8 months of age: daily egg (pasteurised raw whole egg) or rice powder mixed with infant solid foods.

Rice group: 6/35 (17%) infants
Allergic reaction to rice powder
Egg group: 6/40 (15%) infants
Allergic reaction to egg powder
Egg group: 18/35 (51%) infants
Allergic reaction to raw egg

Egg challenge

Fig. 1. Timing of egg introduction in the diet of infants with eczema: trial summary.

References
The Health and Economic Impacts of Early Prevention of Atopic Dermatitis

Jörg Spieldenner
Public Health Nutrition Department
Nestlé Research Center
Lausanne, Switzerland
Jörg.Spieldenner@rdls.nestle.com

Key Messages
Atopic dermatitis is an inflammatory, chronically recurring allergic disorder which exerts a significant economic burden for families of affected children, healthcare systems and society as a whole.

The incidence of atopic dermatitis was significantly reduced when infants (who cannot or were not breast-fed) were fed a specific 100% whey-based partially hydrolyzed infant formula in the first 4 months of life. Early allergy prevention results in significant benefits for health and quality of life of children and their families as well as in economic savings.

The health and economic advantages of allergy prevention should be considered for public healthcare systems and reimbursement agencies.

The prevalence of AD has increased in developing countries over the past decades, with the onset typically occurring in the first year of life [2]. In Europe, the AD prevalence among children is estimated between 10 and 20%, while Latin America and Asia have comparatively high rates [3].

Given the chronic nature of the condition, AD exerts a significant economic burden for families of affected children, healthcare systems and society as a whole [2].

Exclusive breast-feeding for the first three months of life is associated with a protective effect against atopic diseases in children with a family history [4]. It is recommended that infants are exclusively breast-fed for the first 4–6 months of life; however, if it is not possible or desired, infants are given an infant formula instead of or in addition to breast milk. Standard cow’s milk-based infant formulas have been observed to increase an infant’s risk of developing AD [4, 5].

The German Infant Nutritional Intervention (GINI) trial examined the effect of a hydrolyzed infant formula compared to a standard formula on AD in high-risk infants who were not exclusively breast-fed. The study proved that the incidence of atopy significantly decreased when infants were fed a specific 100% whey-based partially hydrolyzed infant formula in the first 4 months of life. The preventive effects lasted up to 6 years of age [4].

Given the economic costs of allergies (in Germany, the total annual cost of AD is EUR 1.2–3.5 billion), health economists have begun to explore the cost-effectiveness of using hydrolyzed formulas for prevention. In the GINI study, the cost-effectiveness of the 100% whey-based partially hydrolyzed infant formula for AD prevention in infants was assessed. The results showed that the consistent use of a specific hydrolyzed formula up to 4 months of age could result in cost savings for German families of up to EUR 14 million over 6 years [4].

Furthermore, a health economics approach was used to estimate the cost-effectiveness of AD prevention in other countries worldwide.

Early allergy prevention results in significant benefits in terms of health and quality of life for children and their families as well as in terms of economic savings. The advantages of allergy prevention should be considered for public healthcare systems and reimbursement agencies to provide recommendations and economic incentives for the use of hydrolyzed infant formulas with proven preventive effect to reduce the incidence of AD.

Table 1. Costs associated with AD from the perspective of the public healthcare system (Ministry of Health, the family and society) [2]

<table>
<thead>
<tr>
<th>Country</th>
<th>Cohort, n</th>
<th>Avoided cases of AD using NAN HA vs. standard formula, n</th>
<th>Burden of disease</th>
<th>Cost savings per case of AD from the family perspective</th>
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<tr>
<td>France</td>
<td>185,298</td>
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Table 2. AD outcomes for a partially hydrolyzed whey formula vs. a standard formula and associated cost savings [6]

References