Purpose of the Study. Feeding extensively or partially hydrolyzed formulas to infants might reduce their risk of developing allergic disorders, but the scope of benefit remains unclear. The authors sought to assess the preventive effect of different hydrolyzed formulas versus cow’s milk in a prospective study among high-risk infants.

Study Population. The subjects were 2252 infants with hereditary risk of atopy, defined as at least 1 biological parent or sibling with an allergic disease.

Methods. Infants were randomly assigned at birth, in a blinded manner, to 1 of 4 formulas, ie, cow’s milk formula (CMF), partially hydrolyzed whey formula, extensively hydrolyzed whey formula, or extensively hydrolyzed casein formula (eHF-C). However, all mothers were encouraged to breastfeed exclusively for the first 4 to 6 months. Study formula was provided for the first 6 months. Avoidance of solid foods for the first 4 months was advised, with subsequent avoidance of cow’s milk, eggs, soy, fish, peanuts, nuts, tomatoes, and citrus fruits during the first year. Mothers maintained diaries of milk sources for the first 6 months. Children were examined at 1, 4, 8, and 12 months of age. The primary end point at 1 year of age was the presence of allergic manifestation, which was defined as atopic dermatitis (AD), gastrointestinal manifestations of food allergy, allergic urticaria, or a combination of both. Both immunoglobulin E-mediated and non-immunoglobulin E-mediated reactions were considered for gastrointestinal manifestations of food allergy, and symptoms needed to disappear with elimination of the suspected formula and to recur with challenge for diagnosis. Asthma and allergic rhinitis were excluded from consideration as allergic manifestations, because diagnoses are usually difficult to establish in the first year of life.

Results. Of the 2252 infants enrolled, 889 were exclusively breastfed for the first 3 months, and 418 left before completion of enrollment data, left thereafter, or were excluded because of noncompliance. A total of 945 infants who adhered to the study formula protocol for the entire 12 months remained. Among the hydrolyzed formulas, only eHF-C was associated with a significant decrease in allergic manifestations, compared with CMF. However, when the outcome of AD was analyzed specifically, both eHF-C and partially hydrolyzed whey formula were associated with more favorable outcomes, compared with CMF. A family history of AD was associated with lesser benefit, with only eHF-C approaching statistical significance, compared with CMF ($P = .077$). The results for exclusively breastfed infants were not included in the analysis, because it was not possible to randomize to breastfeeding for ethical reasons and mothers who chose to nurse differed from the mothers of formula-fed infants with respect to important variables, including greater family prevalence of AD, less smoking, and fewer pets.

Conclusions. The expression of allergic diseases in the first year of life is favorably modified by the use of less allergenic milk sources, especially in the absence of a family history of AD. Individual hydrolysate formulas must be studied more extensively in this role.

Reviewer’s Comments. The findings of this study are consistent with various observations on the role of hypoallergenic formulas in ameliorating allergic disease early in life. Of course, this study was not designed to look beyond the first 1 year of life, and most evidence to date suggests that the protective benefits of such early food allergen avoidance are limited to AD and immunologic reactions to food proteins, without significant effects on lifetime risks for asthma and allergic rhinitis.

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THE RELATIONSHIP BETWEEN EXHALED NITRIC OXIDE AND ALLERGIC SENSITIZATION IN A RANDOM SAMPLE OF SCHOOLCHILDREN


Purpose of the Study. To determine whether there is a relationship between levels of exhaled nitric oxide (eNO) and sensitization to common allergens.

Study Population. A convenience sample of 450 schoolchildren (7–12 years of age), of a total random sample of 2504 children in the Netherlands, were enrolled.

Methods. Children were recruited from 7 public schools and were assessed for allergen sensitization with skin prick testing and/or specific immunoglobulin E (IgE) radioallergosorbent testing (RAST) with common environmental allergens, including dust mite, cat, tree, grass, dog, and mold allergens. eNO was measured with a standard protocol. Families were also asked to complete a questionnaire regarding the home environment, family composition, education, and passive smoke exposure. Associations between eNO levels and sensitization to common allergens were analyzed with adjustments for age, gender, gas cooking, unvented water heaters, passive smoke exposure, and having a cold during sampling.

Results. Of the total 450 children studied, 9% had a lifetime history of asthma, with 10% reporting wheeze in the previous year, 8.2% had a history of hay fever, and 29.1% had a history of eczema ever. Of the 319 children who underwent skin prick testing, 29.5% had ≥1 positive test result, 21.9% for indoor allergens and 15% for outdoor allergens. Of the 229 children who underwent specific IgE RAST, 32.3% had ≥1 positive test result, 23.1% for indoor allergens and 21.8% for outdoor allergens. The geometric mean level of eNO was ~1.5 times higher among children sensitized to indoor allergens, compared with nonsensitized children ($P < .05$), and this was increased to 2 times higher when a cutoff value of ≥2 positive tests was used for either indoor or outdoor allergen sensitivity. eNO levels gradually increased with increases in positive allergen tests. There was no association between eNO levels and current pet ownership. The association between allergen sensitization and eNO was much stronger among children with a history of wheezing, compared with children without wheezing (relative increases of 1.24–1.47 among non-wheezeers and 1.56–3.44 among wheezeers).

Discussion. This study found a positive association between eNO levels and levels of allergen sensitization in a random sample of schoolchildren in the Netherlands. The association was stronger among children with sensitization to indoor allergens and children with a history of wheezing. Association with sensitization to outdoor allergens was not as strong, which the authors proposed might be related to the larger particle size of pollens preventing their entry into lower airways. The mechanism of these elevated eNO levels is not known, but the authors proposed that exposure to allergens could lead to inflammatory changes in the lower airway without causing signs of clinical asthma.

Conclusion. The authors concluded that allergen sensitization was associated with elevated levels of eNO in a random sample of children, most without outward signs of asthma.
FOOD ALLERGY

FACTORS ASSOCIATED WITH THE DEVELOPMENT OF PEANUT ALLERGY IN CHILDHOOD


Purpose of the Study. Because peanut allergy has increased in prevalence and is an important cause of life-threatening reactions, the authors sought to investigate possible determinants of peanut allergy.

Study Population. Data were obtained from the Avon Longitudinal Study of Parents and Children. This geographically defined cohort included 13,971 preschool-aged children. Forty-nine of those children had a history of peanut allergy. Thirty-six of those 49 underwent skin testing, and 29 demonstrated positive results. Peanut allergy was confirmed for 23 children with double-blind, placebo-controlled, food challenge.

Methods. Pregnant women were enrolled and questionered about their allergy history before delivery and were given serial questionnaires throughout their children’s infancy and childhood. The authors prospectively identified 49 children with a history of reactions to peanuts. Twenty-three children were then confirmed as being allergic to peanuts with skin testing and double-blind, placebo-controlled, food challenge. There were 2 control groups, including children with eczema in the first 6 months of life whose mothers also had eczema and 140 children without peanut allergy who were randomly selected from the cohort. Cord blood samples stored at birth were retrieved and analyzed for peanut-specific and total immunoglobulin E (IgE) antibody, TNX-901, raises the threshold of sensitivity against most accidental ingestions of peanuts.

Results. Peanut allergy was found to be independently associated with eczematous dermatitis (rash over joints and creases or oozing crusted rash) in the first 6 months of life, intake of soy products, family history of peanut allergy, and the use of skin preparations containing peanut oil. Neither maternal peanut consumption during pregnancy and lactation nor duration of breastfeeding was found to be associated with the development of peanut allergy. Additional evidence not supporting previous concepts of in utero sensitization came from undetectable peanut-specific IgE and normal total IgE levels in cord blood.

Conclusions. Sensitization to peanut antigens appeared to be through inflamed atopic skin, rather than via the gastrointestinal tract, possibly from the use of skin preparations with even trace amounts of peanut oil. With respect to the independent association between intake of soy products and peanut allergy, soy protein fractions have shown homology to major peanut proteins and cross-sensitization could result from exposure to a common T cell epitope.

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EFFECT OF ANTI-IMMUNOGLOBULIN E THERAPY FOR PATIENTS WITH PEANUT ALLERGY


Purpose of the Study. To determine whether subcutaneous administration of a humanized anti-immunoglobulin E (IgE) antibody, TNX-901, raises the threshold of sensitivity to peanuts among patients with peanut allergy.

Study Population. Eighty-four patients between 12 and 60 years of age, with a history of allergic reactions to peanuts, total IgE levels between 30 and 1000 IU/mL, positive skin prick tests for peanuts, and documented reactions with formal peanut challenge at the start of the study, were studied.

Methods. A randomized, double-blind, placebo-controlled, dose-range study was performed. During the screening process, peanut allergy was confirmed and the threshold for reactivity was determined with a double-blind, placebo-controlled, oral food challenge with encapsulated peanut flour. Patients were subsequently randomized to receive subcutaneous injections of placebo or TNX-901 (150, 300, or 450 mg) at 4-week intervals, for a total of 4 doses. Two to 4 weeks after the final injection, a final peanut challenge was performed, to determine the threshold of reactivity to peanuts after the treatments. Serum samples were obtained at 4-week intervals, to monitor trough total IgE levels.

Results. From mean baseline thresholds of sensitivity of 178 to 436 mg of peanut flour in the various groups, the mean increases in the oral food challenge threshold were 710 mg in the placebo group, 913 mg in the group given 150 mg of TNX-901, 1650 mg in the group given 300 mg of TNX-901, and 2627 mg in the group given 450 mg of TNX-901 (P < .001 for comparison of the 450-mg dose with placebo; P < .001 for trend with increasing dose). Patients who received 450 mg had a mean threshold of reactivity of 2805 mg of peanut protein (equivalent to ~9 peanuts), compared with 178 mg (equivalent to one half of a peanut) before the injections.

Conclusions. Subcutaneous administration of TNX-901 increases the threshold of reactivity to peanuts in a dose-dependent manner, which may translate into protection against most accidental ingestions of peanuts.

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Reviewer’s Comments. eNO has been shown in many studies to be a useful marker of inflammation among asthmatics, but this study demonstrated an association between atopy and eNO levels. It has been suggested that eNO may be a useful screening test for asthma, and perhaps some of these asymptomatic atopic patients are evolving asthmatics. Although eNO devices have received Food and Drug Administration approval, their cost has limited their use to research settings to date.

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Reviewer’s Comments. With the increase in peanut allergy and other food allergies, elucidation of risk factors for prevention of sensitization offers new strategies to combat this food allergy epidemic. Allergic sensitization through the skin has also been proposed for the development of asthma and has been demonstrated in mouse models of atopic dermatitis. Additional studies are needed to determine whether topical peanut oil treatment is definitely a risk factor for peanut allergy; however, it seems prudent to avoid the topical use of peanut oil-containing products among children with atopic dermatitis. The finding of soy consumption being associated with peanut allergy may be attributable to the increased likelihood of food-allergic children receiving soy products, rather than a specific association with peanut allergy. Confirmation of this association is needed.
THE RELATIONSHIP BETWEEN EXHALED NITRIC OXIDE AND ALLERGIC SENSITIZATION IN A RANDOM SAMPLE OF SCHOOLCHILDREN

Mary Beth Bollinger

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