FOOD ALLERGY AND ATOPIC DERMATITIS IN INFANCY: AN EPIDEMIOLOGIC STUDY


Purpose of the Study. To examine the relationship between atopic dermatitis and IgE-mediated food allergy in infancy.

Study Population. A birth cohort of 620 infants from the Melbourne Atopy Cohort Study, a cohort with a family history of eczema, asthma, hay fever, or immediate food allergy in a parent or sibling.

Methods. A total of 487 children had complete data including skin-prick tests to evaluate IgE-mediated food allergy to cow’s milk, egg, and peanut at the age of 1 year. Participants were grouped as no atopic dermatitis (group 0) or in quartiles of increasing severity of atopic dermatitis (groups 1–4) quantified by days of topical steroid use as (groups 1–4) quantified by days of topical steroid use as

Results. The cumulative prevalence of atopic dermatitis was 28.9% by 12 months of age (10.3% of the cohort of moderate severity). As atopic dermatitis severity increased, so did the prevalence of IgE-mediated food allergy (group 0: 40 of 346; group 1: 6 of 36; group 2: 8 of 35; group 3: 12 of 35; group 4: 24 of 35; \( \chi^2 = 76; P < 10^{-6} \)). The frequency of reported adverse food reactions was as follows: group 0, 43 of 346; group 1, 4 of 36; group 2, 8 of 35; group 3, 5 of 35; group 4, 13 of 35 (\( \chi^2 = 17; P = 0.002 \)). The relative risk of an infant with atopic dermatitis having IgE-mediated food allergy is 5.9 for the most severely affected group.

Conclusions. Atopic dermatitis is common in infancy. There is a strong association between IgE-mediated food allergy and atopic dermatitis in this age group.

Reviewer’s Comments. Studies using double-blind, placebo-controlled food challenges show that nearly 40% of infants and young children with severe atopic dermatitis have food allergy. This epidemiologic study focusing on children <1 year of age supports the association of IgE-mediated food sensitization with a history of atopic dermatitis. Therefore, evaluation for food allergies should be considered in infants with severe atopic dermatitis.

JULIE WANG, MD
SCOTT H. SICHERER, MD
New York, NY

LATE ECZEMATOUS REACTIONS TO FOOD IN CHILDREN WITH ATOPIC DERMATITIS


Purpose of the Study. To evaluate the frequency of late-phase atopic dermatitis (AD) reactions to foods during double-blind placebo-controlled food challenges (DBPCCFs) and correlate the results with food-specific IgE and patch tests.

Study Population. Sixty-four children aged 1 to 10 years (median: 2 years) with mild to severe AD evaluated in an outpatient dermatology and allergy department in Germany.

Methods. The inclusion criterion was suspicion of food-related AD by parents and/or a referring physician. The children underwent testing for food-specific IgE (n = 64). Allergen patch testing (APT) to suspected foods was performed if they did not have a rash on their back (n = 41). The first day was an incremental food challenge up to a full serving as tolerated, and on the second day the children were given a full dose of the food/placebo. The children were observed for 48 hours after the challenges. Reactions occurring within 6 hours were considered immediate, and those occurring after >6 hours were considered late reactions.

Results. A total of 106 food challenges were performed to milk, egg, wheat, or soy, with 64% of the children reacting to at least 1 food; of those who reacted, 83% reacted to only 1 food, 15% reacted to 2 foods, and 1 child reacted to 3 foods. The most common trigger was egg (62%), followed by milk (47%) and wheat and soy (35% each). Immediate reactions occurred in 88% of the challenges. Late AD reactions were seen in 28 of 49 (57%) of positive challenges. Sensitivity of history in predicting immediate reactions was only 54%, and for late reactions only 25%; reactions to milk had the highest sensitivity (50–67%), and soy had the lowest (0%). In general, sensitivity (77% vs 68%), specificity (60% vs 50%), and positive predictive values (57% vs 33%) were higher for immediate reactions versus late reactions. Diagnostic accuracy of food-specific serum IgE was greater for children <2 years old. There was no difference in sensitivity (67%) or specificity (38%) of APT for predicting immediate or late AD reactions. The positive predictive value of APT was greater for immediate reactions (38% vs 24%). It is notable that 19% of patients reacted on day 2 of the challenge, having previously tolerated the food on day 1.

Conclusion. Food allergy should be considered in any child with AD who is not responding to standard therapy,
with DBPCFCs still considered the “gold standard” for this diagnosis.

**Reviewers’ Comments.** This study adds support to the current literature demonstrating a link between food allergy and AD. The interesting finding of late reactions observed in this study should be considered, because most observation periods after food challenges are not generally that long.

**LAURA GOBER, MD**

**MARY BETH BOLLINGER, DO**

**Baltimore, MD**

**LYMPHOID NODULAR HYPERPLASIA AND COW’S MILK HYPERSENSITIVITY IN CHILDREN WITH CHRONIC CONSTIPATION**


**Purpose of the Study.** To investigate the incidence of cow’s milk allergy as evidenced by milk challenge and the findings of endoscopic and immunohistochemical examinations in children with chronic and refractory constipation.

**Study Population.** Thirty-five children aged 3 to 15 years with recalcitrant constipation and 15 control subjects.

**Methods.** All children underwent colonoscopy with visual inspection for lymphoid nodular hyperplasia. Mucosal samples were taken from the terminal ileum, cecum, transverse colon, and rectum. Biopsy specimens were evaluated for the presence of lymphoid nodules, lamina propria eosinophils, and mononuclear cells. Immunohistochemical staining was done for CD3 T cells, αδ and γδ T-cell receptor–bearing intraepithelial lymphocytes, and HLA-DR expression. Subjects were placed on a 4-week milk-elimination diet. Other recommendations included a fiber-rich diet and medical treatment with lactulose and sodium picosulfate. For those who responded to elimination, milk was used as a challenge in the ensuing 4-week period. Total serum concentrations of IgA and IgE were measured.

**Results.** Lymphoid nodular hyperplasia was the most prominent endoscopic finding and was detected in 46% of subjects. During the period of milk elimination/supportive medication, 83% of subjects remitted. Relapse occurred in 34% of children after challenge with milk. These children had significantly higher densities of intraepithelial γδ+ T cells (P < .001) in biopsy samples from the terminal ileum.

**Conclusions.** The authors concluded that these results indicate formal evidence of cow’s milk allergy in children with chronic constipation.

**Reviewer’s Comments.** It is fairly common that parents blame cow’s milk formulas for constipation. This study showed that a subset of children (those with higher densities of intraepithelial γδ+ T cells in the terminal ileum) whose constipation improved with a regimen that included cow’s milk avoidance had a relapse of constipation when reexposed to cow’s milk. These results are intriguing and suggest an immunologic link but do not provide formal evidence of cow’s milk allergy. Proof of cow’s milk hypersensitivity would require demonstration of specific recognition of cow’s milk protein by the immune system.

**JOHN E. DUPLANTIER, MD**

**Indianapolis, IN**

**CORRELATION OF INITIAL FOOD REACTIONS TO OBSERVED REACTIONS ON CHALLENGES**


**Purpose of the Study.** Allergic reactions from food can range from mild urticaria to fatal anaphylaxis. There are no clinical or laboratory features that can be used to predict the severity of a subsequent allergic reaction. This study evaluates whether the organ system or the specific food involved in the initial allergic reaction predicts the outcome of a subsequent oral food challenge.

**Study Population.** All food-sensitive children with a history of a food-allergic reaction and a positive skin-test result who underwent food challenges at the Children’s Hospital of Philadelphia (Philadelphia, PA) over a 5-year period.

**Methods.** Open food challenges were offered to all patients with a history of food-allergic reactions and positive skin-test results. If the initial reaction was thought to be significant, the challenge was offered 1 year after their last reaction; if the initial reaction was equivocal, the challenge was performed earlier. The specific food, initial symptom on presentation, and reaction on open challenge were recorded and evaluated retrospectively.

**Results.** A total of 413 of 998 food challenges were positive. Milk, egg, and peanut accounted for 83% of the positive challenges. Milk, egg, and peanut were also more likely than soy or wheat to cause a multiorgan system reaction on challenge. Patients were most likely to experience symptoms similar to those experienced during their initial presentation. Allergy-test results did not reliably predict the severity of a reaction.

**Conclusions.** Milk, egg, and peanut are the most common foods associated with food challenges. A patient typically will experience a similar reaction on reexposure to the initial allergen. However, multiorgan system reactions can occur after any initial clinical presentation, with milk, egg, and peanut causing a greater proportion of multiorgan system reactions than other foods.

**Reviewer’s Comments.** Although subsequent food-allergic reactions were similar to previous ones, more severe reactions can occur. Many patients erroneously believe that subsequent reactions will automatically be more severe over time and this study dispels that notion. However, the results also support the instruction to families that subsequent reactions could be more severe. In the same context, the study results highlight the importance of educating patients on food-allergen avoidance and how to identify and treat allergic reactions, including the use of self-injectable epinephrine.

**HELEN SKOLNICK, MD**

**Princeton, NJ**

**PREDICTION OF THE DEVELOPMENT OF TOLERANCE TO MILK IN CHILDREN WITH COW’S MILK HYPERSENSITIVITY**


**Purpose of the Study.** To investigate whether the development of tolerance to cow’s milk (CM) by the age of 4 years can be predicted with a skin-prick test (SPT) and measurements of total or specific IgE in the serum taken at the time of diagnosis of CM hypersensitivity (CMH).

**Study Population and Methods.** Infants with immediate (n = 95) or delayed (n = 67) challenge reactions to CM...
# Late Eczematous Reactions to Food in Children With Atopic Dermatitis

Laura Gober and Mary Beth Bollinger

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