

Patterns of care and referral in children with atopic dermatitis and concern for food allergy

MICHELE M. THOMPSON, SUSAN J. TOFTE, ERIC L. SIMPSON & JON M. HANIFIN

Department of Dermatology, Oregon Health and Science University, Portland, Oregon

ABSTRACT: Although many providers believe that up to 30% of atopic dermatitis (AD) is food induced, food challenge studies show that food-induced eczematous reactions are rare. When food allergy is suggested to cause AD, it often leads to allergy testing with a high false-positivity rate, in turn further focusing parents on food allergy. Study subjects were children less than 11 years old with AD and food allergy suspicion. Prior diagnoses, provider, and testing patterns were assessed by questionnaire given to the parents. Thirty-eight patients with AD were enrolled. Most subject's parents suspected food allergy induced AD. Initial skin diagnoses were made by pediatricians (79%) and family practitioners (18%) as eczema. Allergy was suggested by providers as cause for AD in 63% of the present study's patients. Seventy-nine percent had allergy testing. Greater than 90% of parents claimed their children had food allergy and food-induced AD. Sixty-six percent had positive food allergy tests and 37% had definite history of immediate IgE reactions to food. The majority of this population had allergy suggested as causative for eczema by their primary care provider and were subsequently evaluated by allergist and allergy testing. Consensus about the role of food allergy between the different providers of AD in children would result in more effective, efficient, and less costly health care.

KEYWORDS: atopic dermatitis/eczema, food allergy, food challenge testing

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease that significantly impacts patients, their families, and the healthcare system. It affects 7–17% of children and the prevalence has been increasing (1,2). The disease usually begins in the first year of life and is characterized by intense itching and eczematous lesions in a characteristic distribution (3). Affected children experience sleep loss, embarrassment, and impaired social and educational adjustment (4). AD has considerable social and economic consequences for patients, families, and the healthcare system (5–7). In 1993 Lapidus and colleagues estimated an annual national cost of \$364 million for the treatment of AD in

children (5). More recent cost analyses have found that AD in pediatric patients has total third-party payer costs of \$.9 to \$3.8 billion per year (8).

The etiology of AD is unknown but it is thought to involve genetic predisposition, immune/inflammatory dysregulation, and epidermal barrier dysfunction, combined with environmental exacerbants. The relationship between food allergy and AD is confusing and a source of controversy among physicians. Many sources describe foods as "exacerbating factors" and some suggest that food allergy is part of the pathogenesis of AD (9), whereas others assert that there is little evidence for allergic mechanisms playing a pathogenetic role (10). Most agree that food allergy is found more often in AD as shown by estimates of 30–40% prevalence in AD children versus 6% of normal children (11–13). Disagreement exists in the ability of food ingestion to induce the eczematous lesions of AD; most dermatologists believe this is rare, whereas pediatricians

Address correspondence and reprint requests to: Michele M. Thompson, MD, Oregon Health & Science University (OP06), 3181 SW Sam Jackson Park Road, Portland, OR 97239–3098, or email: thompsmi@ohsu.

and allergists consider it to be more common (14). Double blind placebo-controlled food challenge is the gold standard for detecting food allergy, and studies using this test show widely conflicting data regarding the generation of AD from food. Many of the positive studies fail to distinguish between the two very different skin morphologies of urticaria (consistent with an immediate IgE reaction) and eczema (15,16; also see Rowlands et al., this issue). When the more chronic eczematous lesions of AD are evaluated, food-induced AD is rare (16, also see Rowlands et al., this issue).

Parents are typically focused on foods and food allergy as contributors to their child's AD. Children with AD often undergo extensive food allergy and general allergy testing, which is costly and fraught with a high false-positivity rate (16,17; also see Rowlands et al., this issue). Falsely positive, questionably relevant test results lead parents to erroneously believe food allergy is causing their child's eczema. Restriction diets follow and often divert the focus away from proper skin care, leading at times to nutritional deficiency (17–19). In Resnick's study, over 40% of primary care providers emphasized the possible role of food allergy (13).

In a university-based AD clinic, the present authors noted a high percentage of parents attributing food allergy as a cause of their child's eczema. The present authors hypothesized that parents are conditioned by nondermatologic practitioners to focus on allergy as causative of their child's eczema. Seeking explanation, the present authors assessed the primary patterns of diagnosis, referral, and testing in children with AD and food allergy concern. The present authors also sought to estimate the percentage of patients in this highly selective population with true food allergy defined as rapid onset IgE-mediated reactions after food ingestion.

Methods

The present authors performed a cross-sectional study, recruiting subjects from the Oregon Health and Science University (OHSU) Department of Dermatology General Clinic and the Clinical Trials Unit during a 3-month period in 2001. All patients included in the present study were ≥ 11 years old with an established diagnosis of AD as defined by standard criteria (3), and all carried a suspicion of food allergy. Suspicion of food allergy was established by chart documentation, parental recall, or evidence of previous radioallergosorbent test (RAST) or skin prick test (SPT), regardless of test result. Demographics and allergy test results were abstracted

Do you or did you ever feel that food contributes to your child's eczema?
 Do you or did you ever feel that food allergy contributes to your child's eczema?
 At what age did your child's skin problem first appear?
 Has your child ever had an allergic reaction to a food or foods? ☐ yes ☐ no

If so, which food(s)?
 What reaction occurred? a. hives b. lip or face swelling
 c. swelling/tightening in mouth/throat d. chest tightening, wheezing or cough
 e. vomiting, diarrhea or cramping f. worsening of eczema
 If you chose f., please describe _____
 How quickly after eating did the allergic reaction occur? _____

Has the child had any type of testing for allergy? If so what test?
 What diagnosis did the child's doctor first give to the skin problem?
 a. eczema e. seborrheic dermatitis (cradle cap)
 b. food allergy f. ichthyosis
 c. atopic dermatitis g. allergy (what type?)
 d. scabies h. other _____

Why type of health care professional made that initial diagnosis?
 a. family practitioner d. dermatologist
 b. pediatrician e. allergist
 c. nurse f. other _____

Was allergy ever suggested as a possible cause of your child's skin problem?
 If yes, by whom? _____

Has the child been seen by an allergist or allergy-focused doctor? Please specify.

Have you restricted foods? If yes, which? _____

FIG. 1. Food allergy questionnaire.

from patient clinical records. One dermatologist (JMH) performed all of the baseline exams. Prior diagnoses, provider, and testing patterns were assessed using a questionnaire that was verbally administered by one of the present authors (MMT) to all subjects' parents (FIG. 1). Age of onset, initial diagnoses, provider information, allergy testing, and dietary restriction information were all obtained from this questionnaire. Additionally, parents were asked if allergy had been suggested as a cause of their child's skin ailments and, if so, by whom. This study was approved by the OHSU Institutional Review Board.

Food allergy as defined by a rapid-onset, IgE-mediated reaction to food was established by a point grading system based on parental history with three possible outcomes: definite, probable, and possible food allergy (FIG. 2) (20). Fifteen points were given for the presence of one or more of the following reactions: lip or face swelling, urticaria, nausea or vomiting, wheezing, and/or respiratory distress. Five points were given for each of the following categories: (a) reaction happening more than once with the same food; (b) reaction happening within 30 min of ingesting the food; (c) food causing reaction was milk, egg, soy, wheat, peanut, or seafood. A sum of 0–30 points was possible. The outcome variables – definite, probable, and possible food allergies – were defined as having a sum of 25 points or greater, 16–25 points, or 0–15 points, respectively.

15 points (Major criteria)

one or more of the following reactions occur upon food ingestion:

lip or face swelling, urticaria, nausea or vomiting, wheezing or respiratory distress

5 points (Minor criteria)

For each of the following:

- a) the reaction has happened more than once with the same food
- b) the reaction happened within 30 minutes of ingesting the food
- c) the food that caused the reaction was: milk, egg, soy, wheat, peanut or seafood

Sum of points determines grading category

≥ 25 points = *definite* food allergy reaction (major criteria and ≥ 2 minor criteria)

≥ 15–26 points = *probable* food allergy reaction (must have major criteria)

≥ 0–15 points = *possible* food allergy reaction (with out major criteria)

FIG. 2. Grading criteria for history of food allergy defined as immediate IgE reaction to food.

Statistical analyses were performed using spss statistical software version 10.0 (SPSS, Chicago, IL). Descriptive statistics were presented as mean ± standard deviation or frequencies.

Results

Thirty-eight patients with moderate to severe, early-onset AD were enrolled. Mean age was 4.8 years and mean age of onset of AD was 4.2 months. Fifty-eight percent of the present study subjects were female; 76% were Caucasian, 22% Asian, and 3% Hispanic. Ninety-one percent had a family history of atopy. Mean baseline exams scores were 3.4 for severity and 3.6 for extent on a 0–5 scale (Table 1).

Greater than 90% of parents claimed that their children had food allergy and food-induced AD. Sixty-six percent (25 of 38) had positive food allergy tests (RAST or SPT) and 37% had definite history of immediate IgE reactions to food according to the present authors' criteria (Table 2).

The correct initial skin diagnosis of "eczema" (58%) or AD(16%) was made in the majority of cases prior to the present authors' evaluation (Table 3). These diagnoses were made largely by pediatricians (79%) and family practitioners (18%) (Table 4). No dermatologists made the initial diagnosis in the present series. Varied other initial diagnoses were given that included food allergy (8%), seborrheic dermatitis (5%), and others (26%), which included: baby acne (8%), "newborn skin" (5%), "dry skin"

Table 1. Demographic information in children with AD and parental concern for food allergy (*N* = 38)

Age (year, mean ± SD)	4.8 ± 3
Age of onset (months, mean ± SD)	4.2 ± 4
Gender	
Female	22 (58%)
Male	16 (42%)
Race (<i>n</i> = 37)	
Caucasian	28 (76%)
Asian	8 (22%)
Hispanic	1 (3%)
Family history of atopy (<i>n</i> = 33)	30 (91%)
Baseline exam scores (<i>n</i> = 30)	
Severity score (mean ± SD)	3.4 ± 1
Extent score (mean ± SD)	3.6 ± 1

Severity and extent scores range from 0 to 5 with 1 mild and 5 severe.

Table 2. Estimate of true food allergy based on history in children with AD and parental food allergy concern (*N* = 38)

Definite	14 (37%)
Probable	10 (26%)
Possible	14 (37%)

Table 3. Initial diagnoses of skin problems made in children with AD (*N* = 38)

Eczema	22 (58%)
Atopic dermatitis	6 (16%)
Food allergy	3 (8%)
Seborrheic dermatitis	2 (5%)
Other ^a	10 (26%)

Some children were initially given more than one diagnosis. ^a"Other" diagnoses included: baby acne(8%), "newborn skin" (5%), "dry skin" 5%, "rash" 5%, infection (3%), and general dermatitis(3%).

Table 4. Providers who made the initial diagnoses in children with AD and food allergy concern

Pediatrician	30 (79%)
Family practitioner	7 (18%)
Nurse	1 (3%)

(5%), "rash" (5%), infection (3%), and general dermatitis (3%).

Parental response to the present authors' questionnaire indicated that allergy was mentioned as a possible cause for AD in 63% of the present authors' patients. This consideration was given by

Table 5. Parental recall of physician advice that allergy may contribute to their child's AD (*N* = 38)

Allergy causation suggested	24 (63%)
Provider type suggesting allergy (<i>N</i> = 24)	
Pediatrician	14 (58%)
Family practitioner	4 (17%)
Allergist	4 (17%)
Naturopath	2 (8%)
Dermatologist	1 (4%)

Table 6. Allergist visits, allergy testing, and food restriction in children with AD (*N* = 38)

Visited an allergist	27 (71%)
Allergy testing	30 (79%)
Food restriction (<i>N</i> = 37)	33 (89%)

pediatricians (58%), family practitioners (17%), allergists (17%), naturopathic practitioners (8%), and dermatologists (4%) (Table 5). Seventy-one percent of children had been seen by an allergist and 79% had allergy testing (60% RAST, 60% SPT, and 17% open food challenge test). Eighty-nine percent of patients had a food-restricted diet at some time from their diagnosis of AD (Table 6).

Discussion

In this population of children with AD selected for suspicion of food allergy, 37% had historical evidence of a definite immediate IgE reaction to foods. This corresponds well to estimates of food allergy frequency in other university-based clinics (12,15). The present authors' patients were generally quite severe, referred because of problems controlling their skin disease. Mean severity and extent scores were 3.4 and 3.6 on a 0–5 scale, using a grading system established many years ago in conjunction with the present study's AD evaluation forms. A majority of children (79%) were tested for food allergy and had positive test results (66% of all children in the present study and 83% of the 30 children tested). The providers' focus on allergy likely contributed to the high percentage of allergy tests performed. Positive tests reinforce a parent's concentration on food allergy, especially if the relevance and the high false-positivity in allergy testing in AD were not adequately explained (15).

Children included in the present study were largely White (76%) and Asian (22%). Hispanic (3%) and African American children were not fully represented. This reflects the small sample size of

the present study and the population demographic of urban Portland, Oregon. Furthermore, many in the present study population were recruited from the present authors' Clinical Trials Unit. These subjects may well come from families with greater resources and higher socioeconomic and educational status than the general population of Oregon. Accordingly, these families may also be more likely to seek and to be able to afford additional providers such as allergists and naturopathic practitioners, as well as the testing associated with these visits.

The present authors found that providers told a majority (63%) of parents that allergy could be causing their child's eczema. As in previous reports, primary care providers were much more likely than dermatologists to focus on allergy as a contributor to AD (13). These data suggest that the providers' suggestion of food allergy may influence development of a similar parental focus leading to expensive testing, subsequent food restriction, and a diminished emphasis on appropriate skin care.

It has been shown that interspecialty differences affect outcomes and health care costs in childhood AD (13). Managed care often dictates that patients see a primary care provider before a specialist. The present study's data reflect this; pediatricians or family practitioners made nearly all of the initial diagnoses of AD (Table 4). The outcome of the initial diagnostic visit is paramount for a chronic disease like AD because this is when the trajectories of perception and treatment are established. From this visit, many patients subsequently may see an allergist or dermatologist or a naturopath. Each encounter proposes different explanations and approaches to AD.

Emphasis on food allergy in AD, as in the present study subjects and many of their providers, is often to the detriment of patients because it deters from proper skin therapy, encourages increased testing and costs, food restriction and, at times, nutritional deficiency (17–19). The present authors' subjects had both a high rate of allergy testing (79%) and food restriction (89%), although only one-third had definite historical evidence of food allergy. Even in the presence of an immediate IgE reaction to food, food challenge studies evaluating for eczematous lesions are rarely positive (15, also see Rowlands et al., this issue). The immediate urticarial responses of true food allergy are different from and not contributory to the more chronic, slow-onset eczematous plaques of AD. This fact is missing from the minds of many parents and practitioners. A clear explanation that, despite the elimination of food items, AD flares

will occur and that the eczema will chronically relapse would help parents understand the disease.

Communication of proper skin care and known trigger factors such as overheating, stress, viral infections, irritants, and xerosis will help optimize parental effort (21). Consensus between generalists, pediatricians, allergists, and dermatologists on the infrequent role of food allergy in the development of AD would also streamline patient care. The lack of such agreement contributes to misperception, misguided, and ineffective treatment (13).

The lack of consensus among practitioners understandably results from the conflicting literature on food allergy and its relationship to AD. Sampson and colleagues assert the role of foods in the development of AD (14); however, these studies were flawed in that the eczematous lesions of AD were not used as an outcome – rather a rapid-onset (2 hours) pruritic, erythematous, morbiliform eruption was considered to be evidence of worsening AD (10). One study tested for eczematous lesions with food ingestion and found that food-worsened AD was rare (Rowlands et al., this issue). There is little evidence in the literature that allergy participates in the development of AD. When true food allergies are present, total clearance of dermatitis with allergen avoidance is rare (10). Furthermore, restriction of allergenic foods in early development does not prevent AD in children. Studies that evaluated avoidance of food allergens starting in utero with pregnant mothers, following through lactation with the infant, and then further in the children up to the age of 3 years, found that by age 7 years there was no difference in the incidence of AD or food allergy from that of the control (22).

Controversy often exists within medicine and between providers, but this particular debate further confuses patients and parents in what is already a frustrating chronic disease. Studies within eczema support groups show that patients and parents express frustration at being told different and conflicting facts about AD by providers (23). Consensus on the optimal approaches to AD and the lack of a significant food role should be established among all physicians.

In our survey, many parents asserted that it appeared obvious to them that their child's skin rash could be related to foods. Others reported observing their child's eczema get worse with certain foods, in the absence of an immediate IgE reaction. Many of these presumed "food allergies" are caused by contact urticaria or primary irritant dermatitis, especially on the face, and are more common in children with AD (10,24). These entities are immunologically distinct from AD but

similar enough clinically that parents and nondermatologists might consider them to be the lesions of AD. Parents and patients have a tendency to focus on foods when it is not clear what is causing their ailment. In studies of acute urticaria in adults, a majority suspected food allergy, yet it was found in less than 1% of the patients (25,26). It is often easier to explain to peers, teachers, and other children that "my child has allergies" versus attempting to explain the often confusing diagnosis of AD.

With a study such as the present, parental reporting can be subjective and influenced by recall bias intrinsic to a survey design. Another approach is to use physician documentation or physician questionnaires, but these patients represent multiple healthcare systems and this type of chart review would have been cumbersome for this small pilot study. Additionally, physicians do not always document the entire advice given in a patient visit. Recall bias would also plague physician questionnaires. The grading criteria for true food allergy defined as immediate IgE reaction to foods (FIG. 2) is not a validated method of food allergy detection; however, the present authors feel it can be a useful, practical, noninvasive tool for clinical assessment. Ideally, a prospective trial comparing this method with a double-blind placebo-controlled food challenge would establish this method's validity, although such a study would have cost and recruitment obstacles. The questionnaire did not ask parents if they initially mentioned food allergy concerns to their primary care provider before they were advised by the physician that allergy could be contributing to their child's eczema. Parents may have presented this belief and prompted the physician to agree with their explanation.

Conclusion

In this small sample of mild to moderate AD in children with suspicion of food allergy, the present authors found that roughly one-third had strong historical evidence of food allergy and that the majority had allergy suggested, as a cause of their eczema, by a primary care physician. Consensus about the role of food allergy between the different providers of AD in children would result in more effective, efficient, and less costly health care.

References

1. Laughter D, Istvan JA, Tofte SJ, Hanifin JM. The prevalence of atopic dermatitis in Oregon schoolchildren. *J Am Acad Dermatol* 2000; **43**: 649–655.

2. Larsen FS, Hanifin JM. Epidemiology of atopic dermatitis. *Immunol Allergy Clin North Am* 2002; **22**: 1–24.
3. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venerol (Stockholm) Suppl* 1980; **92**: 44–47.
4. Crossen JR. Psychological assessment of treatment of patients with atopic dermatitis. *Dermatol Ther* 1996; **1**: 94–103.
5. Lapidus CS, Schwarz DF, Honig PJ. Atopic dermatitis in children: who cares? Who pays? *J Am Acad Dermatol* 1993; **28**: 699–703.
6. Su JC, Kemp AS, Varigos GA, Nolan TM. Atopic eczema: its impact on the family and financial cost. *Arch Dis Child* 1997; **76**: 159–162.
7. Herd RM, Tidman MJ, Prescott RJ, Hunter JAA. The cost of atopic eczema. *Br J Dermatol* 1996; **135**: 20–23.
8. Ellis CN, Drake LA, Prendergast MM, et al. Cost of atopic dermatitis and eczema in the United States. *J Am Acad Dermatol* 2002; **46**: 361–370.
9. Borkowski TA, Sampson HA. A combined dermatology and allergy approach to the management of suspected food allergy. *Dermatol Ther* 1996; **1**: 30–50.
10. Halbert AR, Weston WL, Morelli JG. Atopic dermatitis: is it an allergic disease? *J Am Acad Dermatol* 1995; **33**: 1008–1018.
11. Sampson HA. 93 Adverse reactions to foods. In: Middleton E Jr., Reed CE, Ellis EF, Adkinson NF Jr., Yunginger JW, Busse WW, ed. *Allergy principles and practice*, 4th ed. St. Louis: Mosby; 1661–1686.
12. Eigenmann PA, Sicherer SH, Borkowski TA, Cohen BA, Sampson HA. Prevalence of IgE-mediated food allergy among children with atopic dermatitis. *Pediatrics* 1998; **101**: e8.
13. Resnick SD, Hornung R, Konrad TR. A comparison of dermatologist and generalists: management of childhood atopic dermatitis. *Arch Dermatol* 1996; **132**: 1047–1052.
14. Sampson HA, McCaskill C. Food hypersensitivity and atopic dermatitis: evaluation of 113 patients. *J Pediatr* 1985; **107**: 669–675.
15. Burks AW, Mallory SB, Williams LW, Shirrell MA. Atopic dermatitis: clinical relevance of food hypersensitivity reactions. *J Pediatr* 1988; **113**: 447–451.
16. Sampson HA, Albergo R. Comparison of results of skin tests, RAST, and double-blind, placebo-controlled food challenges in children with atopic dermatitis. *J Allergy Clin Immunol* 1984; **74**: 26–33.
17. Liu T, Howard RM, Mancini AJ et al. Kwashiorkor in the United States: fad diets, perceived and true milk allergy, and nutritional ignorance. *Arch Dermatol* 2001; **137**: 630–636.
18. David TJ, Waddinton E, Stanton RHJ. Nutritional hazards of elimination diets in children with atopic dermatitis. *Arch Dis Child* 1984; **59**: 323–325.
19. Lloyd-Still JD. Chronic diarrhea of childhood and the misuse of elimination diets. *J Pediatr* 1979; **95**: 10–13.
20. Thompson MM, Hanifin JM. Effective therapy of childhood atopic dermatitis allays food allergy concerns. *J Am Acad Dermatol* 2005; **53**(2 Suppl 2): S214–219.
21. Hanifin JM. Critical evaluation of food and mite allergy in the management of atopic dermatitis. *J Dermatol* 1997; **24**: 495–503.
22. Zeiger RS, Heller S. The development and prediction of atopy in high-risk children: follow-up at age seven years in a prospective randomized study of combined maternal and infant food allergen avoidance. *J Allergy Clin Immunol* 1995; 1179–1190.
23. Diamond SF. A qualitative study of archival data from an internet self-help group for people living with atopic dermatitis. Thesis for MA in psychology, May 2000, Saybrook, San Francisco, CA.
24. Webber SA, Graham-Brown RAC, Hutchingson PE, et al. Dietary manipulation in childhood atopic dermatitis. *Br J Dermatol* 1989; **121**: 91–98.
25. Zuberbier T, Ifflander J, Semmler C, Henz BM. Acute urticaria: clinical aspects and therapeutic responsiveness. *Acta Derm Venereol* 1996; **76**: 295–297.
26. Aoki T, Kojima M, Horiko T. Acute urticaria: history and natural course of 50 cases. *J Dermatol* 1994; **21**: 73–77.