Skin prick testing in atopic eczema: atopic to what and at what age?

Kam Lun Hon, Shuxin Susan Wang, Wing Lam Wong, Wing Kwan Poon, Ka Yi Mak, Ting Fan Leung

Hong Kong, China

Original article

Background: **Atopic eczema is a common and distressing disease. This study aimed to review the age-dependent pattern of atopic sensitization to food and aeroallergens in patients with eczema by skin prick testing.**

Methods: **The results of skin prick test (SPT), serum IgE, bronchial challenge test, and family history of atopy in eczema patients seen at a pediatric dermatology clinic were reviewed.**

Results: **SPT results were available in 816 eczema patients. In these patients, 90% had atopic sensitization to at least one aeroallergen, 69% to at least one food allergen, and 94% to at least one allergen by SPT. Together with a family history of atopy in parents or siblings and a personal history of airway atopies, 97% and 99.8% of the patients were atopic, respectively. Bronchial hyper-reactivity (BHR) was demonstrated in 44% of 339 patients. Aeroallergen was more prevalent than food allergen sensitization among children older than 10 years. The mites (*D. pteronysissnus, D. farinae* and *Blomia Tropicalis*) were the most prevalent allergens regardless of age and BHR, but *D. pteronysissnus* and *D. farinae* sensitization were more prevalent among BHR-positive patients. Beef is the least sensitized food protein in all ages.**

Conclusions: **The majority of patients with eczema are atopic to aeroallergens. The mites (*D. pteronysissnus*, *D. farinae* and *Blomia Tropicalis*) are the most prevalent allergens regardless of age and BHR.**

World J Pediatr 2012;8(2):164-168

Key words: **aeroallergens; atopic dermatitis; eczema; food allergens; IgE; skin prick test**

Introduction

Childhood eczema is a distressing disease associated with atopy.[1,2] Disease onset is usually before 5 years of age in the majority of patients.[1,3] The presence of atopy, according to the theory of atopic march, implies that young children with eczema may develop airway allergy such as asthma or allergic rhinitis later in life.[4,5] Atopy is defined clinically (personal or family history of eczema, asthma or allergic rhinitis) and by laboratory tests (such as positive skin prick reaction to common food and aeroallergens or elevated serum IgE levels above laboratory reference range for age).[6-9] It is important to understand what allergens are prevalent in the triggering and mediation of the atopic process.[10,11] In a study involving 90 patients with eczema, dust mite sensitization was found to be more prevalent in older children than infants.[8] Cow's milk sensitization only occurred in one-tenth of these patients. Prevalence of sensitization to common aeroallergens, but not food allergens, was generally higher in children beyond 5 years of age. It was also shown that young infants were generally naive to aeroallergens but became sensitized to the *D. Pteronyssinus* in the next 12 months of age beyond infancy.[9] Furthermore, 80% of these infants were not sensitized to cow's milk and none sensitized to soybean. This study aimed to review the age-dependent pattern of atopic sensitization to food and aeroallergens in patients with eczema by skin prick test (SPT).

Methods

We reviewed all new referrals and existing patients diagnosed with eczema at the pediatric dermatology clinic of a teaching hospital between 1999 and 2010.

Author Affiliations: Department of Pediatrics, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, China (Hon KL, Wang SS, Wong WL, Poon WK, Mak KY, Leung TF)

Corresponding Author: Dr. Kam-lun Ellis Hon, Department of Pediatrics, The Chinese University of Hong Kong, 6/F, Clinical Science Building, Prince of Wales Hospital, Shatin, Hong Kong, China (Tel: 852 2632 2859; Fax: 852 2636 0020; Email: ehon@hotmail.com/ehon@cuhk.edu.hk)

doi: 10.1007/s12519-012-0354-4

Eczema was diagnosed according to the criteria proposed by Hanifin and Rajka.[12] The results of SPT of standard common food and aeroallergens[8,13,14] and serum IgE as well as personnel and family history of atopy in first degree relatives were reviewed. SPT is routinely performed for patients by trained staff, using diluent (negative control) and histamine solution (10 mg/mL; positive control) and standardized food and aeroallergen extracts, including dust mites, cockroach, cat and dog danders, beef, egg white, egg yolk, cow's milk, soybean, peanut, almond, crab, shrimp, lobster, mixed shellfish, tomato, orange and mixed fish (ALK Abelló, Round Rock, Texas). This panel of common food and aeroallergen extracts was determined and regularly reviewed by the staff of medical and pediatric services to be relevant to the local setting. Reactions were considered positive if the wheal was at least 3 mm greater than that of diluent, and was further classified as 1+ (3-5 mm), 2+ (6-8 mm), 3+ or more (≥9 mm). The patients discontinued all pharmacotherapy (antihistamines and/or steroids) at least 3 days before SPT. Data on bronchial challenge test (BCT) with methacholine inhalation were available in older children who were subjected to this test.[15] Children with non-specific dermatitis or dermatosis were excluded from analysis. The review was approved by the Clinical Research Ethics Committee of our University.

Data were expressed as proportion or mean and standard deviation (SD) unless otherwise stated. The chi-square test was used to compare proportions. Multiple linear or logistic regression was used to evaluate whether allergen sensitization was associated with age or bronchial hyper-reactivity (BHR) by BCT. All comparisons were made by two-tailed test, and *P* values less than 0.05 were considered statistically significant.

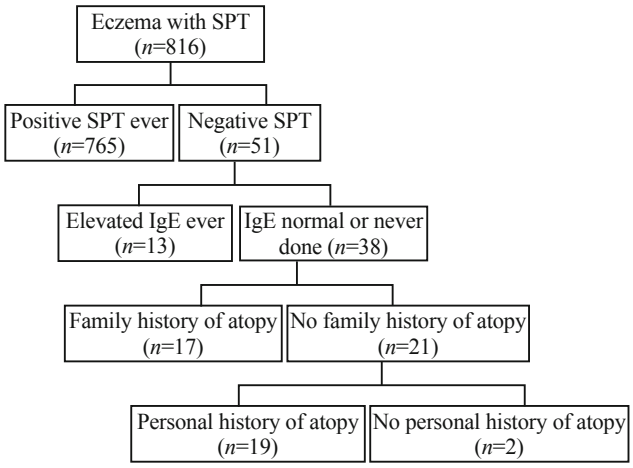

Fig. 1. Skin prick test (SPT), IgE, family history and personal history of atopy in eczema patients. Clinical evidence of atopy includes family history of atopy (eczema, asthma or allergic rhinitis) in first degree relatives (parents and siblings) and personal history of asthma or allergic rhinitis.

Results

Totally 1129 eczema patients (644 males, 57%) born between April 1980 and July 2009 were reviewed, most of them were followed at least once per year until adulthood (18 years of age). Data of the patients were assessed as of April 2010; SPT results were available in 816 (72%) patients (Fig. 1). Ages of patients at time of SPT (10.3±5.0 years) were used for analysis. Totally 765 (94%) of 816 patients had atopic sensitization to at least one allergen by SPT, 648 (90%) of 723 patients to at least one aeroallergen, and 391 (69%) of 568 patients to at least one food allergen.

Serum IgE for age was also tested in 633 (78%) of the patients. It was elevated in 13 (25%) of the remaining 51 patients who were SPT negative (Fig. 1). Family history of atopy in first degree relatives was present in 17 patients whose IgE was normal or not tested ever. Nineteen of the remaining 21 patients without any family history of atopy in first degree relatives had personal history of airway atopy.

Paired results of methacholine BCT with SPT were available in 339 patients and positive in 44% (Fig. 2). The mites (*D. pteronysissnus*, *D. farinae* and *Blomia Tropicalis*) were the most prevalent allergens regardless of age and BHR of patients. Dust mites (*D. pteronyssinus* and *D. farinae*) and "10 tree mix" sensitizations were more prevalent among the patients with BHR shown by BCT (Table 1). Aeroallergen sensitization was more prevalent than food allergens among older children with eczema (Table 2). Ten of the 14 commonly studied aeroallergens were significantly prevalent in older children (≥10 years old), but such age-dependent change in prevalence for food allergens was not observed. Indeed, the prevalence of egg white, egg yolk and peanut sensitization was significantly lowered with age. Apart from the mites,

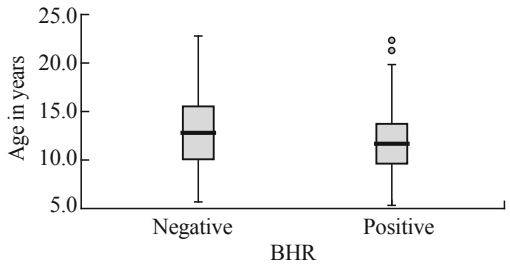

Fig. 2. Age distribution of patients with or without bronchial hyperreactivity (BHR). The mean ages for eczema patients with negative or positive bronchial challenge testing results were 12.9 and 11.8 years, respectively (*P*=0.020).

Table 1. Food and aeroallergen sensitization in eczema patients with and without bronchial hyper-responsiveness (BHR)

Variables	No BHR (*n*=189)	BHR (*n*=150)	Pearson chi-square	OR (95% CI)
Male gender	101 (53.4%)	81 (50.9%)	0.918	0.98 (0.64-1.50)
SPT positive for aeroallergen	+ *vs.* -			
D. pteronyssinus	157 *vs.* 18 (89.7%)	125 *vs.* 5 (96.2%)	0.035	0.35 (0.13-0.97)
D. farinae	146 *vs.* 18 (89.0%)	109 *vs.* 3 (97.3%)	0.011	0.22 (0.06-0.78)
House dust	135 *vs.* 23 (85.4%)	92 *vs.* 12 (88.5%)	0.482	1.31 (0.62-2.76)
Molds, mixed	14 *vs.* 38 (26.9%)	20 *vs.* 40 (33.3%)	0.462	0.74 (0.33-1.66)
Aspergillus fumigatus	29 *vs.* 129 (18.4%)	20 *vs.* 84 (19.2%)	0.859	0.94 (0.50-1.78)
Bermuda grass	19 *vs.* 155 (10.9%)	20 *vs.* 107 (15.7%)	0.218	0.66 (0.33-1.29)
10 tree mix*	2 *vs.* 41 (4.7%)	10 *vs.* 33 (23.3%)	0.013	0.16 (0.03-0.79)
Blomia tropicalis	27 *vs.* 7 (79.4%)	30 *vs.* 3 (90.9%)	0.187	0.39 (0.09-1.64)
Cockroach, mixed†	66 *vs.* 109 (37.7%)	53 *vs.* 77 (40.8%)	0.589	0.88 (0.55-1.40)
Cat fur	60 *vs.* 115 (34.3%)	56 *vs.* 74 (43.1%)	0.118	0.69 (0.43-1.10)
Dog hair	34 *vs.* 141 (19.4%)	23 *vs.* 105 (18.0%)	0.748	1.10 (0.61-1.98)
Cladosporium	40 *vs.* 84 (32.3%)	25 *vs.* 48 (34.2%)	0.774	0.91 (0.50-1.69)
Alternaria	27 *vs.* 97 (21.8%)	14 *vs.* 58 (19.4%)	0.699	1.15 (0.56-2.38)
Penicillium notatum	35 *vs.* 89 (28.2%)	19 *vs.* 53 (26.4%)	0.781	1.10 (0.57-2.11)
SPT positive for food allergen	+ *vs.* -			
Egg white	39 *vs.* 121 (24.4%)	33 *vs.* 72 (31.4%)	0.207	0.70 (0.41-1.22)
Egg yolk	41 *vs.* 117 (25.9%)	31 *vs.* 73 (29.8%)	0.494	0.83 (0.48-1.43)
Cow's milk	15 *vs.* 145 (9.4%)	5 *vs.* 100 (4.8%)	0.164	2.07 (0.73-5.88)
Soyabean	7 *vs.* 30 (18.9%)	7 *vs.* 28 (20.0%)	0.908	0.93 (0.29-3.00)
Wheat, whole	5 *vs.* 32 (13.5%)	5 *vs.* 30 (14.3%)	1.000	0.94 (0.25-3.57)
Peanut	42 *vs.* 118 (26.3%)	32 *vs.* 73 (30.5%)	0.453	0.81 (0.47-1.40)
Almond	9 *vs.* 25 (26.5%)	7 *vs.* 26 (21.2%)	0.614	1.34 (0.43-4.14)
Salmon	27 *vs.* 131 (17.1%)	14 *vs.* 88 (13.7%)	0.468	1.30 (0.64-2.61)
Fish, mixed‡	3 *vs.* 34 (8.1%)	9 *vs.* 26 (25.7%)	0.060	0.26 (0.06-1.04)
Orange	2 *vs.* 30 (6.3%)	3 *vs.* 28 (9.7%)	0.672	0.62 (0.10-4.00)
Tomato	2 *vs.* 33 (5.7%)	2 *vs.* 31 (6.1%)	1.000	0.94 (0.13-7.08)
Beef	14 *vs.* 145 (8.8%)	6 *vs.* 92 (6.1%)	0.436	1.48 (0.55-3.99)
Shellfish, mixed§	73 *vs.* 61 (54.5%)	42 *vs.* 40 (51.2%)	0.641	1.14 (0.66-1.98)

*: 10 tree mix includes alder, ash, beech, birch, elm, history, maple, oak, poplar, and sycamore; †: Cockroach mix includes American and German types; ‡: Fish mix includes flounder, cod, and halibut; §: Shellfish mix includes crab, shrimp, lobster, and oyster. *P*=0.043, 0.018, and 0.024 for *D. pteronyssinus*, *D. farinae*, and 10 tree mix, respectively. SPT: skin prick test.

Table 2. Skin prick test (SPT) in children of two age groups

Variables	<10 y (*n* = 376)	≥10 y (*n* = 441)	OR (95% CI)	*P* value
Age, y (mean ± SD)	5.90 ± 2.84	14.10 ± 2.74	NA	<0.001
Male gender	226 (60.1%)	243 (55.1%)	0.815 (0.616-1.077)	0.149
SPT for aeroallergens	+ *vs.* -			
D. pteronyssinus	275 *vs.* 71 (79.5%)	346 *vs.* 30 (92.0%)	0.336 (0.213-0.529)	<0.001
D. farinae	218 *vs.* 67 (76.5%)	267 *vs.* 19 (93.4%)	0.232 (0.135-0.397)	<0.001
House dust	175 *vs.* 73 (70.6%)	215 *vs.* 38 (85.0%)	0.424 (0.273-0.658)	<0.001
Molds, mixed	35 *vs.* 174 (16.7%)	55 *vs.* 141 (28.1%)	0.516 (0.320-0.832)	0.007
Aspergillus fumigatus	20 *vs.* 228 (8.1%)	55 *vs.* 197 (21.8%)	0.314 (0.182-0.542)	<0.001
Bermuda grass	38 *vs.* 294 (11.4%)	65 *vs.* 302 (17.7%)	0.601 (0.390-0.924)	0.020
10 tree mix*	14 *vs.* 161 (8.0%)	17 *vs.* 126 (11.9%)	0.645 (0.306-1.357)	0.248
Blomia tropicalis	54 *vs.* 59 (47.8%)	59 *vs.* 14 (80.8%)	0.217 (0.109-0.433)	<0.001
Cockroach, mixed†	84 *vs.* 261 (24.3%)	169 *vs.* 206 (45.1%)	0.392 (0.285-0.540)	<0.001
Cat fur	88 *vs.* 257 (25.5%)	165 *vs.* 210 (44.0%)	0.436 (0.318-0.598)	<0.001
Dog hair	44 *vs.* 299 (12.8%)	77 *vs.* 296 (20.6%)	0.566 (0.378-0.847)	0.006
Cladosporium	35 *vs.* 104 (25.2%)	59 *vs.* 123 (32.4%)	0.702 (0.429-1.149)	0.159
Alternaria	19 *vs.* 119 (13.8%)	40 *vs.* 141 (22.1%)	0.563 (0.309-1.024)	0.060
Penicillium notatum	27 *vs.* 111 (19.6%)	52 *vs.* 129 (28.7%)	0.603 (0.355-1.025)	0.062
SPT for food allergens	+ *vs.* -			
Egg white	106 *vs.* 160 (39.8%)	68 *vs.* 221 (23.5%)	2.153 (1.493-3.105)	<0.001
Egg yolk	96 *vs.* 152 (38.7%)	67 *vs.* 186 (26.5%)	1.753 (1.201-2.560)	0.004
Cow's milk	36 *vs.* 240 (13.0%)	30 *vs.* 259 (10.4%)	1.295 (0.773-2.168)	0.326
Soyabean	17 *vs.* 125 (12.0%)	18 *vs.* 95 (15.9%)	0.718 (0.351-1.467)	0.363
Wheat, whole	16 *vs.* 125 (11.3%)	11 *vs.* 102 (9.7%)	1.187 (0.527-2.671)	0.679
Peanut	90 *vs.* 185 (32.7%)	70 *vs.* 219 (24.2%)	1.522 (1.053-2.200)	0.026
Almond	22 *vs.* 91 (19.5%)	19 *vs.* 54 (26.0%)	0.687 (0.341-1.384)	0.293
Salmon	39 *vs.* 207 (15.9%)	42 *vs.* 210 (16.7%)	0.942 (0.585-1.517)	0.806
Fish, mixed‡	23 *vs.* 119 (16.2%)	16 *vs.* 97 (14.2%)	1.172 (0.586-2.341)	0.654
Orange	5 *vs.* 107 (4.5%)	5 *vs.* 63 (7.4%)	0.589 (0.164-2.114)	0.417
Tomato	8 *vs.* 130 (5.8%)	5 *vs.* 103 (4.6%)	1.268 (0.403-3.991)	0.685
Beef	23 *vs.* 244 (8.6%)	24 *vs.* 259 (8.5%)	1.017 (0.559-1.850)	0.955
Shellfish, mixed§	75 *vs.* 94 (44.4%)	108 *vs.* 119 (47.6%)	0.879 (0.589-1.311)	0.528

*: 10 tree mix includes alder, ash, beech, birch, elm, history, maple, oak, poplar, and sycamore; †: Cockroach mix includes American and German types; ‡: Fish mix includes flounder, cod, and halibut; §: Shellfish mix includes crab, shrimp, lobster, and oyster. NA: not available.

the prevalence of cockroach and cat fur sensitization was also increased with age in Hong Kong. No such phenomenon was observed with dog fur sensitization. The prevalence of beef sensitization was the lowest among all the commonly studied proteins.

Discussion

We studied more than 800 children and adolescents over a 10-year period and found that 95% of them were atopic, shown by positive skin prick test or detection of elevated serum IgE level for age. Together with a family history of atopy in parents or siblings and a personal history of airway atopies, 99.8% of the patients were atopic. Thus for all practical purposes, eczema is an atopic disease. SPT and IgE are objective and readily available laboratory tests. Family history of atopy is useful and important but is limited if the patient is adopted, has no sibling, or has siblings of young age. Personal history of atopy other than eczema is particularly unreliable in young children, especially when atopy has not yet "marched".

Eczema is primarily a systemic atopic disease with skin manifestations, rather than a skin disease with systemic associations.[5] The mites (*D. pteronysissnus*, *D. farinae* and *Blomia Tropicalis*) were the most prevalent allergens regardless of age and BHR. Our data suggest that the pattern of atopic sensitization is age-dependent. Children older than 10 years of age are generally sensitized to a number of common aeroallergens, whereas younger children are more likely to be sensitized to egg and peanut. In previous studies, similar patterns of sensitization were documented in Hong Kong and Singapore.[8,9,13,14,16-19] In addition to the common dust mites *D. pteronysissnus* and *D. farinae*, these studies also demonstrated the prevalence of *Blomia Tropicalis* sensitization as an important aeroallergen in Southeast Asia. Apart from the mites, the prevalence of cockroach and cat fur sensitization was also high and increased with age in Hong Kong. These are well documented aeroallergens in an urban environment. Nevertheless, such phenomenon was not observed in dog fur. The prevalence of beef sensitization was lowest among all the commonly studied food proteins. The prevalence of wheat and cow's milk protein sensitization was also relatively low in Hong Kong. These foods, however, were commonly avoided by the Hong Kong parents.[13,14]

Furthermore, BHR (as a surrogate of airway atopy) was detected by BCT in about 40% of patients and was associated with the dust mites and "10 tree mix" sensitizations. It is assumed that airway allergies would manifest as the child grows and his/her eczema symptoms improve or regress. Indeed, the theory of "atopic march" views eczema as a systemic atopic disease with skin manifestations in early childhood, and subsequent airway manifestations.[4,8,9] As the prevalence of food and aeroallergen sensitization may vary significantly from place to place, more studies should be performed at different localities and with more test allergens.

The limitations of determination of airway atopy in young children vary. First, young children are unable to perform respiratory studies consistently. Second, the symptoms of airway atopy are difficult to ascertain in young children. Rhinitis, wheezing and coughs are common confounding symptoms of upper respiratory tract infections. Thus, the symptoms of atopic march might not be apparent at young ages. Also, we did not quantify disease severity in this study because relapse of eczema makes quantification at any single time point irrelevant. Ideally, a large cohort of young children with eczema should be prospectively evaluated and followed till adulthood to determine the nature of atopic sensitization. Importantly, our study demonstrates that aeroallergen rather than food allergen sensitization is more prevalent in older children with eczema and those with BHR. Older patients with eczema are sensitized to common aeroallergens and have BHR.[8,9] Conversely, most (62%) of the patients with BCT performed had no evidence of BHR in this study, supporting the fact that not all eczema patients had airway allergies.[20]

In conclusion, the mites (*D. pteronysissnus*, *D. farinae* and *Blomia Tropicalis*) are the most prevalent allergens. The majority of patients with eczema display dermatologic evidence of atopy at young ages. They are more often sensitized to common aeroallergens than food allergens and some may develop BHR as they become older.

Funding: None.
Ethical approval: Clinical Research Ethics Committee as mentioned in methods.
Competing interest: None.
Contributors: Hon KL was the principal author. Wang SS analyzed the data. Wong WL, Poon WK, and Mak KY assisted in data collection. Leung TF reviewed the manuscript.

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Received December 13, 2010
Accepted after revision March 17, 2011