Pediatr Allergy Immunol 2010: 21: 920–926
DOI: 10.1111/j.1399-3038.2010.00994.x

PEDIATRIC ALLERGY AND IMMUNOLOGY

Establishing the diagnosis of peanut allergy in children never exposed to peanut or with an uncertain history: a cross-Canada study

Ben-Shoshan M, Kagan R, Primeau M-N, Alizadehfar R, Turnbull E, Harada L, Dufresne C, Allen M, Joseph L, St. Pierre Y, Clarke A. Establishing the diagnosis of peanut allergy in children never exposed to peanut or with an uncertain history: a cross-Canada study.
Pediatr Allergy Immunol 2010: 21: 920–926.

The diagnosis of peanut allergy (PA) can be complex especially in children never exposed to peanut or with an uncertain history. The aim of the study is to determine which diagnostic algorithms are used by Canadian allergists in such children. Children 1–17 yrs old never exposed to peanut or with an uncertain history having an allergist-confirmed diagnosis of PA were recruited from the Montreal Children's Hospital (MCH) and allergy advocacy organizations. Data on their clinical history and confirmatory testing were compared to six diagnostic algorithms: I. Skin prick test (SPT) ≥8 mm or specific IgE ≥5 kU/l or positive food challenge (+FC); II. SPT ≥8 or IgE ≥15 or +FC; III. SPT ≥13 or IgE ≥5 or +FC; IV. SPT ≥13 or IgE ≥15 or +FC; V. SPT ≥3 and IgE ≥5 or IgE ≥5 or +FC; VI. SPT ≥3 and IgE ≥15 or IgE ≥15 or +FC. Multivariate logistic regression analysis was used to identify factors associated with the use of each algorithm. Of 497 children recruited, 70% provided full data. The least stringent algorithm, algorithm I, was applied in 81.6% (95% CI, 77–85.6%) of children and the most stringent, algorithm VI, in 42.6% (95% CI, 37.2–48.1%).The factor most associated with the use of all algorithms was diagnosis made at the MCH in those never exposed to peanut. Other factors associated with the use of specific diagnostic algorithms were higher paternal education, longer disease duration, and the presence of hives, asthma, eczema, or other food allergies. Over 18% (95% CI, 14.4–23.0%) of children were diagnosed with PA without fulfilling even the least stringent diagnostic criteria.

Moshe Ben-Shoshan[1], Rhoda Kagan[2], Marie-Noël Primeau[1], Reza Alizadehfar[1], Elizabeth Turnbull[3], Laurie Harada[4], Claire Dufresne[5], Mary Allen[6], Lawrence Joseph[3,7], Yvan St. Pierre[3] and Ann Clarke[3,8]

[1]Division of Pediatric Allergy and Clinical Immunology, Department of Pediatrics, [2]Division of Allergy and Clinical Immunology, Montreal, Quebec, Canada, [3]Division of Clinical Epidemiology, Department of Medicine, McGill University Health Center, [4]Anaphylaxis Canada (AC), Toronto, Ontario, Canada, [5]Association Québécoise des Allergies Alimentaires (AQAA), Montreal, Quebec, Canada, [6]Allergy/Asthma Information Association (AAIA), Toronto, Ontario, Canada, [7]Department of Epidemiology and Biostatistics, McGill University, [8]Division of Allergy and Clinical Immunology, Department of Medicine, McGill University Health Center, Montreal, Quebec, Canada

Key words: peanut allergy; diagnosis; uncertain history; confirmatory tests; skin prick tests; specific IgE

Moshe Ben-Shoshan, Division of Pediatric Allergy and Clinical Immunology, Department of Pediatrics, McGill University Health Center
Tel.: +514 484 2401
Fax: +514 512 4390
E-mail: daliamoshebs@gmail.com

Accepted 6 January 2010

Up to 8.1% of adults believe that their children have a peanut allergy (PA) (1). However, after evaluation by a physician trained in allergic diseases, only 1–2% of children are actually diagnosed as having a PA (2). Given that PA accounts for the majority of severe food-related allergic reactions, can be induced by trace quantities of peanut, and usually lasts for life (3, 4), it is crucial to properly establish the diagnosis. It is equally important to avoid mislabeling children as allergic to peanut given that the diagnosis carries with it the need for significant dietary restrictions and lifestyle modifications (5). However, diagnostic certainty can be difficult, especially in children with no previous exposure to peanut or with an atypical reaction to peanut (referred to hereafter as an uncertain clinical history).

The diagnostic work-up of suspected PA includes careful review of the patient's history and results of the skin prick test (SPT) (6, 7), serum level of peanut-specific IgE (8, 9), and

Abbreviations: FC, food challenge; MCH, Montreal Children's Hospital; PA, peanut allergy; SPT, skin prick test.

food challenge (FC) (9). A clinical history of a food allergy has only a 50% positive predictive value for clinical allergy (10). In those with no previous peanut exposure or an uncertain clinical history, a single diagnostic test, such as a SPT or peanut-specific IgE level, may not be sufficient to establish the diagnosis (11). Pucar et al. (7) have shown that only 31.3% of children who had no known peanut exposure and a positive SPT were truly allergic to peanut. Although the double-blinded placebo-controlled food challenge (DBPCFC) still represents the 'gold standard' for diagnosing food allergy (7), even it may sometimes be misleading (12).

The aim of this study was to characterize the diagnostic testing done by allergists in children with no previous peanut exposure or with an uncertain clinical history of PA and who were diagnosed by an allergist as allergic to peanut. These diagnostic tests were then compared to a variety of diagnostic criteria, and factors potentially associated with the use of each set of criteria were identified.

Methods

Sampling frame

Children 1–17 yrs old with no known previous peanut exposure or with an uncertain clinical history of PA and diagnosed by an allergist as allergic to peanut were recruited from the Montreal Children's Hospital (MCH) Allergy Clinic and from provincial and national advocacy organizations for food allergic patients including Association Québécoise des Allergies Alimentaires, Anaphylaxis Canada, and the Allergy and Asthma Information Association. Participants from food allergy advocacy organizations were recruited through advertisements placed in the association newsletters, e-bulletins, or at annual association conferences. For participants from the MCH, the medical charts were reviewed to determine how the diagnosis of PA was established. Participants from the associations permitted the research team to request information from their allergist regarding testing performed to diagnose PA. The study was approved by the Research Ethics Board of the McGill University Health Centre.

Data collection

The parents of participating children completed a questionnaire on demographic characteristics, accidental exposure to peanut in the year prior to study entry, history of idiopathic urticaria, and the presence of atopic disorders in the child. Atopy was defined as the presence of either atopic dermatitis, allergic rhinitis, asthma, or food allergy. For children recruited from food allergy advocacy organizations, data on initial and most severe reaction to peanut and family history of atopy were also obtained through the questionnaire; for children recruited from the MCH, these data were obtained through chart review.

An uncertain clinical history of an IgE-mediated reaction to peanut was defined as one mild sign/symptom, a reaction occurring more than 2 h after exposure, a reaction occurring through inhalation of peanut, or a reaction where the food contents were unclear. Pruritus, urticaria, flushing, or rhinoconjunctivitis were defined as mild symptoms; angioedema, throat tightness, gastrointestinal complains, or breathing difficulties (other than wheeze) as moderate; and wheeze, cyanosis, or circulatory collapse as severe (3). In cases where clinical history details were unclear, they were confirmed by telephoning the parents.

Confirmatory tests

Confirmatory tests used in the diagnosis of PA include a SPT, serum peanut-specific IgE, and a FC.

Skin prick test to peanut protein. A SPT is defined as positive if the greatest diameter of the wheal was at least 3 mm larger than the negative control (saline) within 12–15 min of placement (6). The SPT in children recruited from the MCH was performed using the prick technique and glycerinated peanut extract supplied by ALK-Abelló (Hørsholm, Denmark). In this technique, a drop of peanut extract was placed on the skin and a solid-bore smallpox needle (Hollister-Stier, Spokane, WA, USA) was passed through it; histamine phosphate in 50% glycerin served as the positive control and 50% glycerosaline as the negative control. For children recruited from food allergy advocacy associations, only the results of the SPT compared to the negative control were provided and the technique was not specified.

Peanut-specific IgE. The serum level of peanut-specific IgE was measured for children recruited from the MCH by the CAP system Fluoroenzyme Immunoassay (Phadia AB Diagnostics, Uppsala, Sweden). However, children recruited from elsewhere may have had peanut-specific IgE measured through other quantitative methods,

including Turbo RAST (currently HYTECH-288, Hycor Biomedical-Agilent, Garden Grove, CA, USA), Immulite IMMULITE 2000;DPC, Los Angeles, CA, USA), and Hy Tec EIA (Hycor Biomedicals, Kassel, Germany). Information regarding the method used to measure specific IgE levels in participants from food allergy advocacy organizations was not provided.

Oral food challenge to peanut. The DBPCFC is recognized as the gold standard for the diagnosis of PA but is usually reserved for research (7, 8). An open challenge is often preferred in clinical practice as it is less time consuming and labor intensive (13). Open-, single- or double-blinded FCs were performed at the discretion of the treating physician. Oral FCs were not done prospectively, and details were obtained from the data provided.

Diagnostic algorithms

Based on the medical literature, we were able to generate six possible sets of diagnostic criteria or algorithms for establishing the presence of PA (Fig. 1):

I. SPT ≥8 mm or peanut-specific IgE ≥5 kU/l or positive FC (14): Although the sensitivity and negative predictive value of a positive SPT (i.e., wheal diameter ≥3 mm) are ≥95%, the specificity and positive predictive value are <50%, unless the clinical history is convincing (6, 7). Sporik et al. (14) have reported a SPT wheal diameter ≥8 mm to be 100% specific in predicting a positive challenge to peanut in high-risk young children. Bernard et al. (15) suggest that a peanut-specific IgE level ≥5 kU/l may be adequate to diagnose PA. However, both the SPT and peanut-specific IgE thresholds may not be applicable to older peanut-naïve children (14, 15).
II. SPT ≥8 mm or peanut-specific IgE ≥15 kU/l or positive FC (14, 16): Individuals with a peanut-specific IgE ≥15 kU/l have a 95% likelihood of experiencing an allergic reaction upon exposure to peanut (8, 9) and, therefore, this may be a sufficient diagnostic criteria in those who have never had a SPT or when the SPT wheal diameter is <8 mm. However, depending on the prevalence of PA in the population studied, a different diagnostic threshold may be more appropriate (8, 17, 18).
III. SPT ≥13 mm or peanut-specific IgE ≥5 kU/l or positive FC (15, 19): A SPT wheal ≥13 mm was reported to have a specificity of 100% for a positive peanut challenge in children with an atopic background never exposed to peanut (19). If the SPT wheal diameter is <13 mm or a SPT is not done, a peanut-specific IgE ≥5 kU/l may be used to establish the diagnosis (15). However, a lower threshold wheal diameter may be acceptable in peanut-naïve children without an atopic history (20).
IV. SPT ≥13 mm or peanut-specific IgE ≥15 kU/l or positive FC (9, 19): Requiring either a SPT ≥13 mm (21) or a peanut-specific IgE ≥15 kU/l (9) (when the SPT is <13 mm or not done) may further increase diagnostic accuracy.
V. SPT ≥3 mm and a peanut-specific IgE ≥5 kU/l or peanut-specific IgE ≥5 or positive FC (15): Although a SPT ≥3 mm has a specificity and positive predictive value of approximately 50% (6), combining it with a peanut-specific IgE should further increase the diagnostic accuracy.
VI. SPT ≥3 mm and a peanut-specific IgE ≥15 kU/l or peanut-specific IgE ≥15 kU/l or positive FC (9).

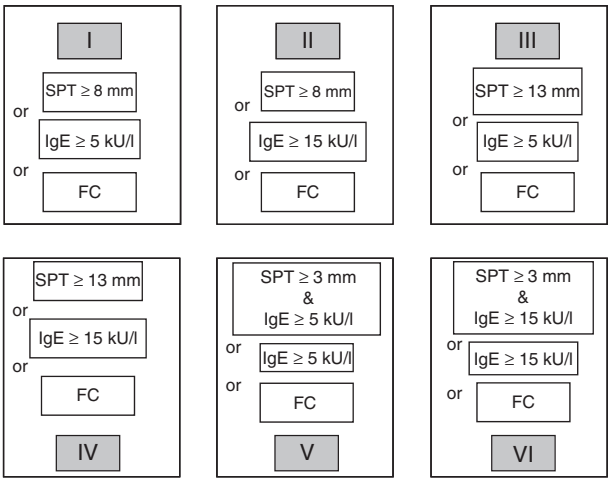

Fig. 1. Algorithms for diagnosing peanut allergy.

Using the data provided by treating allergists, it was possible to determine the percentage of children with an allergist diagnosis of PA fulfilling the criteria for each of the six diagnostic algorithms described above.

Statistical analysis

Descriptive statistics including means, ranges, and standard deviations were generated for all variables. A separate multivariate logistic regression

was conducted for each of six sets of diagnostic criteria and examined whether the testing profile for each child satisfied each set of diagnostic criteria. We considered the following variables as potential predictors of use of each set of criteria: patient's age, gender, parental education (high school, college, university), parental employment status, household structure of family (single vs. non-single parents), atopic features of the patient and/or his parents, presence of siblings with PA, accidental exposures over the year prior to study entry, previous peanut exposure, time interval between initial reaction (if applicable) and study entry, recruitment from the MCH vs. food allergy associations (considered as four categories: MCH patients and never exposed, MCH patients with an uncertain history, association patients and never exposed, and association patients with an uncertain history), and geographic location of treating allergist (urban vs. rural). All these variables were measured at study entry unless otherwise stated. Urban vs. rural location was determined by the first three digits of the allergist's postal code.

Univariate analysis was conducted to identify potential predictors, and multivariate analysis was conducted for those whose allergists and parents provided sufficient data. Comparing univariate to multivariate results allowed us to investigate possible confounding factors.

Results

Four hundred and ninety-seven children were recruited. Complete data regarding confirmatory testing and potential factors associated with the use of a specific algorithm were available in 331 of 497 children recruited (approximately 70% of cases) (Table 1). Participants with incomplete data (on questionnaire or chart review) or with no confirmatory tests results provided by their physicians were

Table 1. Demographics of respondents and non-respondents

	Recruited from Montreal Children's Hospital (n = 214)	Recruited from associations (n = 117)	Non-respondents (n = 166)
Age at baseline, yr*			
Mean (s.d.) [CI]	6.9 (3.7) [6.4, 7.4]	6.8 (3.5) [6.1, 7.4]	6.9 (4.1) [6.2, 7.5]
Range	[1, 17]	[1, 16]	[1, 17]
Age at diagnosis, yr (s.d.) [CI]†	3.0 (2.2) [2.7, 3.3]	3.2 (2.7) [2.7, 3.7]	3.0 (2.5) [2.6, 3.4]
Disease duration, yr (s.d.) [CI]†	3.9 (3.6) [3.4, 4.4]	3.6 (3.2) [3.0, 4.2]	3.9 (3.7) [3.3, 4.5]
Sex, % boys [CI]	54.4 [47.3, 61.3]	60.0 [50.2, 69.2]	59.0 [49.8, 67.8]
Ethnic background of child, % white	87.4 [82.2, 91.5]	96.6 [91.5, 99.1]	N/A
Hives	28.5 [22.6, 35.1]	41.4% [32.3, 50.9]	N/A
Personal atopic history, % [CI]			
Atopic dermatitis	51.9 [45.0, 58.7]	50.9 [41.4, 60.3]	48.7 [40.6, 56.9]
Asthma	53.3 [46.3, 60.1]	57.8 [48.2, 66.9]	46.1 [38.1, 54.3]
Allergic rhinitis	35.5 [29.1, 42.3]	40.5 [31.5, 50.0]	13.0 [8.1, 19.3]
Other food allergies	62.2 [55.3, 68.8]	71.3 [62.1, 79.4]	70.1 [62.2, 77.2]
≥1 atopic comorbidity	87.9 [82.7, 91.9]	90.6 [83.8, 95.2]	88.3 [82.2, 92.9]
Family atopic history (first degree relatives), % [CI]			
Peanut allergy	7.6 [4.4, 12.0]	28.6 [19.9, 38.6]	N/A
≥1 atopic comorbidity	77.5 [71.2, 83.0]	84.0 [75.3, 90.6]	N/A
Uncertain history, % [CI]	55.1 [48.2, 61.9]	33.3 [24.9, 42.6]	47.6 [39.8, 55.5]
Age of parents			
Mother, y (s.d.) [CI]	38.2 (6.0) [37.4, 39.0]	38.7 (5.4) [37.7, 39.7]	N/A
Father, y (s.d.) [CI]	40.3 (6.7) [39.3, 41.2]	40.6 (5.9) [39.5, 41.7]	N/A
Parental education/work status, % [CI]			
Mother			
Completed high school	97.2 [94.0, 99.0]	100 [96.9, 100]	N/A
Completed college	86.0 [80.6, 90.3]	91.5 [84.8, 95.8]	N/A
Completed university	58.4 [51.5, 65.1]	73.5 [64.5, 81.2]	N/A
Employed at baseline	66.4 [59.6, 72.7]	70.9 [61.8, 79.0]	N/A
Father			
Completed high school	93.9 [89.8, 96.7]	95.7 [90.3, 98.6]	N/A
Completed college	77.6 [71.4, 83.0]	81.2 [72.9, 87.8]	N/A
Completed university	55.6 [48.7, 62.4]	61.5 [52.1, 70.4]	N/A
Employed at baseline	87.4 [82.2, 91.5]	93.2 [87.0, 97.0]	N/A
Urban location of treating allergist, % [CI]	100	87.5 [79.9, 93.0]	95.1 [90.5, 97.8]

*Based on age at study entry.
†Based on the earliest of first clinical reaction or first confirmatory test.

defined as non-respondents. There were no meaningful differences between respondents and non-respondents.

Among those with uncertain history, 94.8% had only one mild symptom, 0.9% reported a reaction occurring more than 2 h after exposure, 2.2% were exposed through inhalation, and in 2.1% it was not clear whether the food associated with the reaction contained peanut. The majority of SPT and specific IgE tests were done in MCH (70.1% and 77.4%, respectively). FCs were done in 19 children (5.7%), all diagnosed at the MCH and all were positive.

The percentage of children fulfilling the diagnostic criteria for each algorithm were: 81.6% (95% CI, 77.0–85.6%), 78.5% (95% CI, 73.7–82.8%), 61.0% (95% CI, 55.5–66.3%), 56.5% (95% CI, 51.0–61.9%), 48.0% (95% CI, 42.5–53.6%), and 42.6% (95% CI, 37.2–48.1%) for algorithms I through VI, respectively.

Diagnosis at the MCH of patients never exposed to peanut was associated with all six algorithms [OR of 4.30 (95% CI, 1.83–10.14), 3.69 (95%, CI 1.73–7. 89), 4.71 (95% CI, 2.50–8.88), 5.16 (95% CI, 2.84–9.36), 7.11 (95% CI, 3.91–12.94), and 7.64 (95% CI, 4.31–13.56)] (Table 2).

Diagnosis at the MCH in the presence of an uncertain history was associated with the use of algorithms I and II [OR 2.20 (95% CI, 1.11–4.37) and 2.27 (95% CI, 1.19–4.30)].

Higher paternal education was associated with algorithms I, II, III, and IV [OR of 2.61 (95% CI, 1.41–4.81), 2.72 (95% CI, 1.53–4.83), 1.89 (95% CI, 1.16–3.11), and 2.06 (95% CI, 1.27–3.34)].

Longer disease duration was associated with all algorithms [OR of 1.13 (95% CI, 1.02–1.25), 1.12 (95% CI, 1.02–1.25), 1.11 (95% CI, 1.02–1.20), 1.14 (95% CI, 1.06–1.23), 1.17 (95% CI, 1.08–1.26), and 1.20 (95% CI, 1.11–1.30)].

Hives were associated with algorithms I and III [OR of 2.21 (95% CI, 1.09–4.48) and 1.82 (95% CI, 1.05–3.15)], asthma with algorithm III [OR of 1.85 (95% CI, 1.12–3.06)], eczema with algorithms IV, V, and VI [OR 1.76 (95% CI, 1.08–2.87), OR 1.84 (95% CI, 1.10–3.07), and OR 1.99 (95% CI, 1.19–3.32)], and other food allergies with algorithm V [OR 1.74 (95% CI, 1.02–2.99)].

Additionally, having a working mother was associated with a decreased likelihood of using algorithm VI [OR 0.52 (95% CI, 0.30–0. 89)].

Table 2. Odds ratio and 95% confidence intervals for factors associated with each algorithm

Covariates	OR (95% CI)
Algorithm I: Skin prick test (SPT) ≥8 mm or peanut-specific IgE ≥5 kU/l or positive food challenge (FC)*	
Diagnosed at Montreal Children's Hospital (MCH) and never exposed	4.30 (1.83, 10.14)
Father with university education	2.61 (1.41, 4.81)
Hives	2.21 (1.09, 4.48)
Diagnosed at MCH with an uncertain history	2.20 (1.11, 4.37)
Disease duration	1.13 (1.02, 1.25)
Algorithm II: SPT ≥8 mm or peanut-specific IgE ≥15 kU/l or positive FC*	
Diagnosed at MCH and never exposed	3.69 (1.73, 7.89)
Father with university education	2.72 (1.53, 4.83)
Diagnosed at MCH with an uncertain history	2.27 (1.19, 4.30)
Disease duration	1.12 (1.02, 1.23)
Algorithm III: SPT ≥13 mm or peanut-specific IgE ≥5 kU/l or positive FC*	
Diagnosed at MCH and never exposed	4.71 (2.50, 8.88)
Father with university education	1.89 (1.16, 3.11)
Asthma	1.85 (1.12, 3.06)
Hives	1.82 (1.05, 3.15)
Disease duration	1.11 (1.02, 1.20)
Algorithm IV: SPT ≥13 mm or peanut-specific IgE ≥15 kU/l or positive FC*	
Diagnosed at MCH and never exposed	5.16 (2.84, 9.36)
Father with university education	2.06 (1.27, 3.34)
Eczema	1.76 (1.08, 2.87)
Disease duration	1.14 (1.06, 1.23)
Algorithm V: SPT ≥3 mm and a peanut-specific IgE ≥5 kU/l or peanut-specific IgE ≥5 kU/l or positive FC*	
Diagnosed at MCH and never exposed	7.11 (3.91, 12.94)
Eczema	1.84 (1.10, 3.07)
Other food allergies	1.74 (1.02, 2.99)
Disease duration	1.17 (1.08, 1.26)
Algorithm VI: SPT ≥3 mm and a peanut-specific IgE ≥15 kU/l or peanut-specific IgE ≥15 kU/l or positive FC*	
Diagnosed at MCH and never exposed	7.64 (4.31, 13.56)
Eczema	1.99 (1.19, 3.325)
Disease duration	1.20 (1.11, 1.30)
Mother works	0.52 (0.30, 0.89)

*Only significant associations are reported.

Discussion

This is the first study assessing the applicability of possible algorithms in diagnosing PA in children who were never exposed or had an uncertain history of PA.

Our results suggest that 18.4% of children with such a history were diagnosed by an allergist as having PA without fulfilling even the least stringent diagnostic criteria (among participants, 81.6% met the diagnostic criteria of algorithm I). Based on the most stringent algorithm, algorithm VI, almost 60% did not meet the criteria for PA. We anticipate that this percentage would be much higher had we included children who had been diagnosed as allergic by a physician other than an allergist.

The factor most associated with the use of all algorithms was diagnosis made at the MCH in those with no previous exposure, presumably because of the greater availability of allergen-specific IgE and the FC in a hospital setting (22). It is possible that diagnosis at the MCH in the

presence of an uncertain history was associated only with algorithm I and II because a history suggesting a reaction to peanut, although uncertain, may be perceived as sufficient evidence of allergy and thus physicians may be more likely to use less stringent algorithms.

The observed association between higher paternal education and use of algorithms I, II, III, and IV may be because paternal education is associated with increased awareness of diagnostic tests and demand for testing (23). The association between longer disease duration and algorithms I through VI may be because those with longer duration have had more opportunity to undergo testing to either confirm the diagnosis or assess the emergence of tolerance (24). The known association between severe food allergy and other atopic diseases (25, 26) likely explains our observed association between asthma and algorithm III and eczema and algorithms IV–VI. In the presence of asthma or eczema, physicians are more aggressive in confirming the diagnosis of food allergy as it has major prognostic implications. Interestingly, the presence of PA in the family was not associated with the use of a specific algorithm although the medical literature reports a strong familial aggregation of food allergies, especially among siblings (27) with PA.

Our study has potential limitations. Given that the algorithms we present were not compared to a DBPCFC in a population of children never exposed to peanut or with an uncertain history, it is difficult to state which is the most appropriate and each has shortcomings. It is possible that by relying on physicians' notes and patient recall, we are underestimating the presence of additional symptoms or signs that may have been considered by the treating allergist as evidence of a convincing history of an allergic reaction to peanut and hence, justify not using additional testing. Furthermore, our study population is well educated with a high level of awareness about food allergy (35% of our study population was recruited from food allergy advocacy associations). Our findings may have differed if our sample had been of a lower socioeconomic status or recruited from other sources. Finally, levels of peanut-specific IgE measured outside the MCH might not have been determined through the CAP system Fluoroenzyme Immunoassay, and discrepancies may exist between different assays (28, 29). Because the published allergen-specific IgE thresholds were measured by the CAP system (9), there is a clear advantage in using this system to confirm the diagnosis of PA.

Our findings suggest that although several confirmatory tests are available to establish the diagnosis of PA, full use is not made in a substantial proportion of subjects. Given that specific IgE levels are relatively easily obtained, have high predictive value (9), and are useful as predictors of PA tolerance (24, 30), they should be measured in all children with suspected PA. As the optimal algorithm for diagnosing PA in those with no previous exposure or an uncertain history has not yet been developed, we recommend increased use of existing algorithms requiring both SPT and IgE. Studies assessing the correlation between different diagnostic algorithms and the DBPCFC are required to establish the most appropriate algorithm for diagnosing PA in those with no previous peanut exposure or an uncertain history.

References

1. Leung TF, Yung E, Wong YS, Lam CW, Wong GW. Parent-reported adverse food reactions in Hong Kong Chinese pre-schoolers: epidemiology, clinical spectrum and risk factors. Pediatr Allergy Immunol 2009: 20: 339–46.
2. Rona RJ, Keil T, Summers C, et al. The prevalence of food allergy: a meta-analysis. J Allergy Clin Immunol 2007: 120: 638–46.
3. Hourihane JO, Kilburn SA, Dean P, Warner JO. Clinical characteristics of peanut allergy. Clin Exp Allergy 1997: 27: 634–9.
4. Sicherer SH, Burks AW, Sampson HA. Clinical features of acute allergic reactions to peanut and tree nuts in children. Pediatrics 1998: 102: e6.
5. Avery NJ, King RM, Knight S, Hourihane JO. Assessment of quality of life in children with peanut allergy. Pediatr Allergy Immunol 2003: 14: 378–82.
6. Eigenmann PA, Sampson HA. Interpreting skin prick tests in the evaluation of food allergy in children. Pediatr Allergy Immunol 1998: 9: 186–91.
7. Pucar F, Lim H, Clarke AE. Peanut oral challenge: a retrospective study of 140 patients. Clin Exp Allergy 2001: 31: 40–6.
8. Rancé F, Abbal M, Lauwers-Cances V. Improved screening for peanut allergy by the combined use of skin prick tests and specific IgE assays. J Allergy Clin Immunol 2002: 109: 1027–33.
9. Sampson HA, Ho DG. Relationship between food-specific IgE concentrations and the risk of positive food challenges in children and adolescents. J Allergy Clin Immunol 1997: 100: 444–51.
10. Bock SA, Atkins FM. Patterns of food hypersensitivity during sixteen years of double-blind, placebo-controlled food challenges. J Pediatr 1990: 117: 561–7.
11. Clark AT, Ewan PW. Interpretation of tests for nut allergy in one thousand patients, in relation to allergy or tolerance. Clin Exp Allergy 2003: 33: 1041–5.
12. Vlieg-Boerstra BJ, van der Heide S, Bijleveld CM, Kukler J, Duiverman EJ, Dubois AE. Placebo reactions in double-blind, placebo-controlled food challenges in children. Allergy 2007: 62: 905–12.
13. Baker H, Luyt D, Stern M. Open challenge to nuts in children. Allergy 1999: 54: 79–80.
14. Sporik R, Hill DJ, Hosking CS. Specificity of allergen skin testing in predicting positive open food challenges

to milk, egg and peanut in children. Clin Exp Allergy 2000: 30: 1540–6.
15. Bernard H, Paty E, Mondoulet L, et al. Serological characteristics of peanut allergy in children. Allergy 2003: 58: 1285–92.
16. Hill DJ, Heine RG, Hosking CS. The diagnostic value of skin prick testing in children with food allergy. Pediatr Allergy Immunol 2004: 15: 435–41.
17. Roberts G. Anaphylaxis to foods. Pediatr Allergy Immunol 2007: 18: 543–8.
18. Du TG, Santos A, Roberts G, Fox AT, Smith P, Lack G. The diagnosis of IgE-mediated food allergy in childhood. Pediatr Allergy Immunol 2009: 20: 309–19.
19. Kagan RS, Hayami D, Joseph L, St-Pierre Y, Clarke AE. The predictive value of a positive prick skin test to peanut in atopic, peanut-naïve children. Ann Allergy Asthma Immunol 2003: 90: 640–5.
20. Van GD, Govaere E, Verhamme K, Doli E, De BF. The influence of atopic status and potential risk factors for sensitization on histamine skin reactivity in unselected Belgian children. Pediatr Dermatol 2007: 24: 363–8.
21. Eigenmann PA, Zamora SA. An internet-based survey on the circumstances of food-induced reactions following the diagnosis of IgE-mediated food allergy. Allergy 2002: 57: 449–53.
22. Bock SA, Sampson HA, Atkins FM, Zeiger RS, Lehrer S, Sach SM. Double-blind, placebo-controlled food challenge (DBPCFC) as an office procedure: a manual. J Allergy Clin Immunol 1988: 82: 986–97.
23. Fishbein EG. Predicting paternal involvement with a newborn by attitude toward women's roles. Health Care Women Int 1990: 11: 109–15.
24. Ho MH, Wong WH, Heine RG, Hosking CS, Hill DJ, Allen KJ. Early clinical predictors of remission of peanut allergy in children. J Allergy Clin Immunol 2008: 121: 731–6.
25. Summers CW, Pumphrey RS, Woods CN, McDowell G, Pemberton PW, Arkwright PD. Factors predicting anaphylaxis to peanuts and tree nuts in patients referred to a specialist center. J Allergy Clin Immunol 2008: 121: 632–8.
26. Munoz-Furlong A, Weiss CC. Characteristics of food-allergic patients placing them at risk for a fatal anaphylactic episode. Curr Allergy Asthma Rep 2009: 9: 57–63.
27. Tsai HJ, Kumar R, Pongracic J, et al. Familial aggregation of food allergy and sensitization to food allergens: a family-based study. Clin Exp Allergy 2009: 39: 101–9.
28. Kontis KJ, Chen A, Wang J, Nayak N, Li TM. Performance of a fully automated *in vitro* allergy testing system. Allergol Immunopathol (Madr) 1997: 25: 63–6.
29. Wood RA, Segall N, Ahlstedt S, Williams PB. Accuracy of IgE antibody laboratory results. Ann Allergy Asthma Immunol 2007: 99: 34–41.
30. Skolnick HS, Conover-Walker MK, Koerner CB, Sampson HA, Burks W, Wood RA. The natural history of peanut allergy. J Allergy Clin Immunol 2001: 107: 367–74.