

Original article

Early clinical predictors of remission of peanut allergy in children

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Background: Understanding predictors of clinical remission would assist in clinical management of peanut allergy.

Objective: We sought to determine the early clinical predictors of peanut allergy remission using a longitudinal cohort of young children with peanut allergy.

Methods: Consecutive patients less than 2 years of age with peanut allergy were identified on the basis of skin prick test (SPT) wheal size of 95% positive predictive value or greater. Baseline SPT responses to peanuts, tree nuts, and sesame and serum peanut-specific IgE antibody levels were documented, and follow-up studies were conducted at 1- to 2-year intervals for up to 8 years. Peanut food challenges were performed when SPT responses decreased to less than the 95% positive predictive value for peanut allergy.

Results: SPT wheal diameters to peanut extract of 6 mm or greater (hazard ratio, 2.16; 95% CI, 1.23-3.786; $P = .008$) and peanut-specific IgE antibody of 3 kUA/L or greater (hazard ratio, 2.74; 95% CI, 1.13-6.61; $P = .025$) before the age of 2 years were independent predictors of persistent peanut allergy. Mean SPT wheal diameters of nonremitters increased ($r = 0.31$, $P < .001$), whereas those of remitters decreased ($r = -0.26$, $P = .002$) between 1 and 4 years of age. Twenty-one percent of young children with peanut allergy became clinically tolerant by age 5 years.

Conclusions: Remission of peanut allergy can be predicted by low levels of IgE antibodies to peanut in the first 2 years of life or decreasing levels of IgE sensitization by the age of 3 years. (J Allergy Clin Immunol ■■■■;■■■:■■■-■■■.)

Key words: Peanut allergy, tree nut, sesame, clinical predictors, skin prick test, peanut-specific IgE

Abbreviations used

FEIA: Fluorescent enzyme immunoassay

PPV: Positive predictive value

SPT: Skin prick test

In Australia 1.9% of infants and young children are estimated to have peanut allergy.¹ The prevalence of peanut allergy in childhood in other countries varies between 0.5% and 1.8%.¹⁻⁵ Peanut allergy is estimated to have increased 2-fold in the United States in the 5-year period to 2002^{4,6} and nearly 4-fold in the last decade in the United Kingdom.³ In many Western societies it accounts for the majority of severe food allergy reactions in childhood. In highly sensitized individuals microgram amounts of peanut can precipitate symptoms.⁷⁻¹⁰

Although many food allergies remit in early childhood, only 20% of children with peanut allergy have tolerance.¹¹⁻¹³ These studies suggest that children with tolerance have a lower-level IgE sensitization to peanut from the outset, as well as a lower incidence of other atopic disorders, including asthma, eczema, and hay fever. However, these investigations were cross-sectional and included children of a wide age range, many of whom were already likely to have received diagnoses. No previous study has recruited an exclusively young cohort of children with peanut allergy and followed them longitudinally.

In this longitudinal study a large group of young children with peanut allergy under the care of one pediatric allergist were assessed at regular intervals over a prolonged period. The natural history of peanut allergy and clinical and laboratory features associated with persistence or remission of the disease were investigated.

METHODS

Consecutive children less than 2 years of age referred to the Children's Allergy Centre, Royal Children's Hospital, Melbourne, from 1995 through 2000 and found to have peanut allergy were studied. Peanut allergy was diagnosed if the child had a skin prick test (SPT) diameter of 95% positive predictive value (PPV) or greater for peanut allergy (ie, an SPT response to peanut ≥ 4 mm).¹⁴ Approval for this study was granted by the Royal Children's Hospital Institutional Review Board.

Skin prick tests

SPTs were performed by using a single-head lancet technique on the backs of infants and on the forearms of older children with histamine (1 mg/mL) and commercial allergen extracts (Dome-Hollister-Stier, Spokane, Wash)¹⁵ and read at 10 minutes and 15 minutes, respectively. Diluent solution was used

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as a negative control. Prick-prick tests were performed with fresh nuts where indicated.

Peanut-specific IgE

Where stored serum was available, IgE antibodies to peanut were measured with the CAP system fluorescent enzyme immunoassay (FEIA; Pharmacia, Uppsala, Sweden). The assay had a lower limit of detection of 0.35 kUA/L. Levels of 100 kUA/L or greater were reported as 100 kUA/L. Total serum IgE levels were also determined.

Peanut challenge

Patients were admitted to the allergy department for peanut challenges. On day 1, a smear of commercially prepared peanut butter was applied to the buccal mucosa of the lower lip, and then at 30-minute intervals, a dose of 1/8, 1/4, 1/2, and 1 teaspoon was applied. One teaspoon (5 mL) of smooth peanut butter contains approximately 1.6 g of peanut protein (product information). From day 2 onward, peanut butter was ingested, increasing by 1 teaspoon a day until 5 teaspoons per day was reached, which is equivalent to 8 g of peanut protein per day.¹⁵ From day 2, the challenge was conducted at home, and the child was clinically reviewed by the allergist (DJH) on days 7 and 28. A positive challenge result was recorded if an unequivocal reaction to peanut (ie, urticaria, eczema flare, erythematous rash; vomiting, diarrhea; sneezing, rhinorrhea, stridor, wheeze, cough; or anaphylaxis) was observed within 1 hour of the last challenge dose being administered. A negative challenge result was recorded if normal amounts of peanut were ingested (ie, ≥ 8 g of peanut protein per day for 1 week). An inconclusive challenge result (eg, abdominal pain or nausea without other objective findings) was recorded if the above criteria were not met. If the open challenge was inconclusive, a 4 $\times$ 1 double-blind, placebo-controlled food challenge with peanut butter was administered at 30-minute intervals in the center. The last dose of peanut thought to elicit the adverse symptoms in the open challenge was concealed in a savory food in the double-blind, placebo-controlled food challenge.

Conduct of the study

Patients were reviewed by the same allergist (DJH) at 1- to 2-year intervals. Patients were educated regarding stringent avoidance of dietary peanut, tree nuts, and sesame seeds, including avoiding products labeled "may contain traces of nuts."

At enrollment (median age, 14 months), all children had SPTs for peanut, cow's milk, hen's egg, cashew, hazelnut, sesame (fresh tahini paste), and inhalants (*Dermatophagoides pteronyssinus*, dog dander, cat dander, and *Loxium perenne*). These investigations were repeated at each visit until preschool assessment. At enrollment, parents of 181 patients permitted blood to be taken for laboratory studies.

At the preschool assessment (median age, 4 years), baseline SPTs were repeated, as well as SPTs with extracts of walnut, pecan, brazil nut, and almond, and prick-prick tests with fresh nuts of macadamia, pine, and pistachio were tested. These tests and assessments were repeated at 1- to 2-year intervals until completion of the study.

EpiPen (self-administered adrenaline; Dey Laboratories, Napa, Calif) with appropriate training and education and an Anaphylaxis Action Plan from the Australasian Society of Clinical Immunology and Allergy (www.allergy.org.au) were prescribed to all participants.

Peanut challenges were offered when the SPT wheal diameter became age appropriate less than 95% PPV for peanut, which is less than or equal to 4 mm for children younger than 2 years and less than or equal to 8 mm for children 2 years of age and older, as previously validated in our center.¹⁶

Definitions

IgE food sensitization to peanut, cow's milk, hen's egg, tree nuts (including cashew, hazelnut, walnut, pecan, brazil nut, and almond), and sesame was defined as an SPT wheal size of 3 mm or larger for each allergen.

IgE food allergy to peanut, cow's milk, hen's egg, tree nuts (including cashew, hazelnut, walnut, pecan, brazil nut, and almond), and sesame was defined as an unequivocal clinical reaction within the past 12 months, an SPT of greater than 95% PPV for a positive food challenge, or both, as previously described (an unequivocal reaction was anaphylaxis and/or an urticarial or angioedematous skin eruption and/or acute vomiting with or without diarrhea within 1 hour of ingestion of the food within 3 months of the initial presentation or within 12 months during the conduct of the study).¹⁴⁻¹⁷

At enrollment, the 95% PPV for SPT for cow's milk allergy was 6 mm, for hen's egg allergy was 5 mm, for peanut allergy was 4 mm, and for sesame allergy was 8 mm. After the age of 2 years, these 95% PPVs for SPT for allergy were 8 mm for milk, 7 mm for egg, 8 mm for peanut, and 8 mm for sesame and tree nuts.¹⁴⁻¹⁶ Ninety-five percent PPV for peanut by means of CAP-FEIA was 14 kUA/L or greater.¹⁷

IgE sensitization to inhalants was defined as an SPT wheal size equal to or greater than 3 mm for each allergen.

Statistical analysis

Categorical data of remitters and nonremitters were compared by using the χ^2 test with the Yates correction. Continuous variables were compared by using the Student *t* test or the Mann-Whitney *U* test. Pearson correlation analysis was applied to the sequential time change of SPT sizes for both remitters and nonremitters. By using the Youden index on the receiver operator curve, the best cutoff point of peanut-specific IgE and SPT wheal diameter (<2 years of age) for predicting tolerance was determined. For longitudinal analysis of persistence of peanut allergy, the Kaplan-Meier log-rank test was used for univariate analysis. Cox regression modeling was used for covariate variables of clinical and laboratory characteristics at enrollment and follow-up and to calculate univariate hazard ratios. All statistical analysis was performed with SAS software, version 9.1 (SAS, Inc, Cary, NC).

RESULTS

A total of 297 children were given diagnoses of peanut allergy (mean/median age, 14.1/13.5 months; range, 4-23 months; male/female ratio, 1.9:1) during the study period. Of these, 267 who had come back for subsequent evaluation formed this study population, with a median follow-up of 4.7 years (SD, 2 years). They presented (1) with a history of an adverse reaction to peanut (93 [35%] patients), (2) for investigation of an adverse reaction to other common food allergens (109 [41%] patients), or (3) for investigation of eczema and no history of adverse food reactions (65 [24%] patients). All patients had SPTs of greater than 95% PPV for peanut allergy at enrollment in the study (as per the selection criteria for inclusion in the study).

Enrollment assessment

There was no difference in SPT size to peanut at study entry between peanut allergy remitters compared with nonremitters (Table I). CAP-FEIA results were available for 181 patients. Although all study patients had greater than 95% PPV SPT diameter for peanut allergy (as per study entry criteria), only 29 (16.0%) of 181 patients had peanut-specific IgE levels of 14 kUA/L or greater (95% PPV for IgE-mediated food allergy to peanut by means of CAP-FEIA). Sera were available from 93 patients who had an unequivocal index reaction to peanut before enrollment; only 10 (10.7%) of 93 had peanut-specific IgE levels of 14 kUA/L or greater. All patients with peanut-specific IgE levels of 14 kUA/L or greater were nonremitters.

There was a positive correlation ($r = 0.174$, $P = .02$) between SPT wheal size and specific IgE antibody levels to peanut. The total mean IgE level of 142 kUA/L (SD, 100 kUA/L) versus 54

TABLE I. Comparison of clinical features and laboratory investigations at enrollment (median age, 14 months) of children with transient (remitter) and persistent (nonremitter) peanut allergy

Enrollment variable	Remitter, n = 49 (18.4%)	Nonremitter, n = 218 (81.6%)	P value
Male/female ratio	2:1	1.8:1	NS
Median age (mo [range])	14.4 (6-21.5)	13.8 (4-23)	NS
Mean duration (mo of follow-up [range])	54.5 (20-116)	62.8 (20-137)	NS
Exclusive breast-feeding ≥ 4 mo	35 (71.4%)	148 (67.9%)	NS
Soy ingestion to 2 y	19 (39%)	72 (33%)	NS
History of acute peanut reaction	14 (28.6%)	79 (36.2%)	NS
Severe	2	10	NS
Moderate	4	24	NS
Mild	8	45	NS
Atopic eczema	31 (63.2%)	138 (63.7%)	NS
Egg allergy	35 (71.4%)	141 (64.7%)	NS
Milk allergy	24 (48.9%)	86 (39.4%)	NS
Sensitization to inhalation allergen (SPT ≥ 3 mm)	18 (36.7%)	109 (50.0%)	NS
Median (mean) SPT (mm)	6 (7.3)	7 (7.6)	NS
SPT, peanut ≥ 8 mm	13 (26.5%)	96 (43.8%)	<.05
SPT, peanut ≥ 6 mm	25 (51.0%)	157 (71.7%)	<.01
Median total IgE (U/L [range])	54 (9-522), n = 30	142 (5-2669), n = 151	<.05
Mean (SD) FEIA, peanut-specific IgE (kUA/L)	2.0 (3.2), n = 30	12.2 (22.6), n = 151	<.001
FEIA, peanut-specific IgE ≥ 8 kUA/L	1 (3.33%)	51 (33.8%)	<.01
FEIA, peanut-specific IgE ≥ 3 kUA/L	1 (3.33%)	61 (40.4%)	<.001
Tree nut sensitization	11 (22.4%)	110 (49.5%)	<.01
Tree nut allergy	3 (6.1%)	22 (10.1%)	NS
Sesame sensitization	7 (14.2%)	60 (27.5%)	<.05
Sesame allergy	0	5 (2.3%)	NS

NS, Not significant.

P value of less than .05 is considered significant.

kUA/L (SD, 30 kUA/L; $P < .05$) and mean peanut-specific IgE level of 12.2 kUA/L (SD, 22.6 kUA/L) versus 2.0 kUA/L (SD, 3.2 kUA/L; $P < .001$) were significantly higher in nonremitters than remitters. Nonremitters had higher rates of sensitization to, but not clinical allergy to, cashew, hazelnut, and sesame seed. There was no difference in the incidence of eczema, cow's milk, or hen's egg allergy between the groups.

Preschool assessment

The preschool assessment (median age, 4 years) was completed by 223 (83.5%) of the group, of whom 40 (18%) of 223 remitted (Table II). At this time, the remitters had significantly smaller SPT wheal diameters to peanut and a lower frequency of both sensitization and food allergy to tree nuts and sesame than nonremitters. Although resolution of egg and milk allergy occurred more commonly in remitters, the difference was not significant. Physician-diagnosed asthma requiring prophylactic medication was more frequent in nonremitters than remitters. A greater number of accidental peanut-induced allergic reactions occurred during the study in children with nonremitting peanut allergy than among those who remitted (55/218 [25.2%] vs 4/49 [8.2%], $P < .05$, Table III).

TABLE II. Follow-up assessment of children with peanut allergy at 4 years of age

Follow-up assessment at age 4 y	Remitter, n = 40	Nonremitter, n = 183	P value
Male/female ratio	1.8:1	1.8:1	NS
Median age (mo [range])	46 (37-55)	48 (36-59)	NS
Median SPT diameter (mm)	3	10	<.01
Δ Median SPT diameter 1-4 y (mm)	-3	+3	<.0001
Resolved egg allergy	19/28 (67.9%)	55/119 (46.2%)	NS
Resolved milk allergy	17/19 (89.5%)	47/72 (65.3%)	NS
Current asthma	12 (30%)	124 (67.8%)	<.05
Current atopic eczema	14 (35%)	73 (39.9%)	NS
Tree nut sensitization	8 (17.4%)	139 (73.2%)	<.0001
Multiple tree nut sensitization (≥ 3)	2 (5%)	64 (35%)	<.001
Tree nut allergy	10 (25%)	79 (43.1%)	<.05
Sesame seed sensitization	6 (13%)	54 (29.5%)	<.001
Sesame seed allergy	2 (5%)	30 (16.3%)	<.001

P value of less than .05 is considered significant. NS, Not significant.

TABLE III. Postenrollment accidental peanut reaction

Accidental peanut ingestion	Remitters (n = 49)	Nonremitters (n = 218)	P value
Postenrollment accidental reaction	3 (8.2%)	51 (25.2%)	.005
With prior reaction	1/18 (5.5%)	18/75 (24%)	.005
Without prior reaction	2/31 (6.5%)	33/143 (23.1%)	.008
Mean (range) duration (mo) of follow-up	54.5 (20-116)	62.8 (20-137)	NS
Emergency department attendance caused by peanut	0 (0%)	11 (5%)	NS
Ever used EpiPen	0 (0%)	4 (2%)	NS

P value of less than .05 is considered significant. NS, Not significant.

Longitudinal follow-up

Peanut allergy remitted in 49 patients (median age, 4 years and 3 months; range, 21-96 months; male/female ratio, 2:1). Of the 218 nonremitters, 195 (89%) had SPT wheal sizes to peanut of 95% PPV or greater, and 26 of these 195 had reactions after inadvertent peanut ingestion in the 12 months before their last assessment. The remaining 24 nonremitters had SPT wheal sizes of less than 95% PPV for peanut allergy; 6 of these had an inadvertent peanut reaction in the previous year, 13 had persistent peanut allergy confirmed by means of positive oral peanut challenge, and 5 patients who underwent food challenge were considered inconclusive. The median age from the diagnosis to remission was 42 months. Cumulative probability of the loss of peanut allergy was 13.2% at 3 years of age, 21.4% at 5 years of age, and 34.2% at 7 years of age.

Sequential changes in SPT responses to peanut extract

In Fig 1 the SPT wheal size at each age of the 49 patients whose peanut allergy remitted by completion of the study is compared with that of the 218 nonremitters. For the children enrolled by 1 year of age, the median SPT sizes were smaller in remitters (6 mm vs 7 mm), although not significantly. Mean SPT wheal

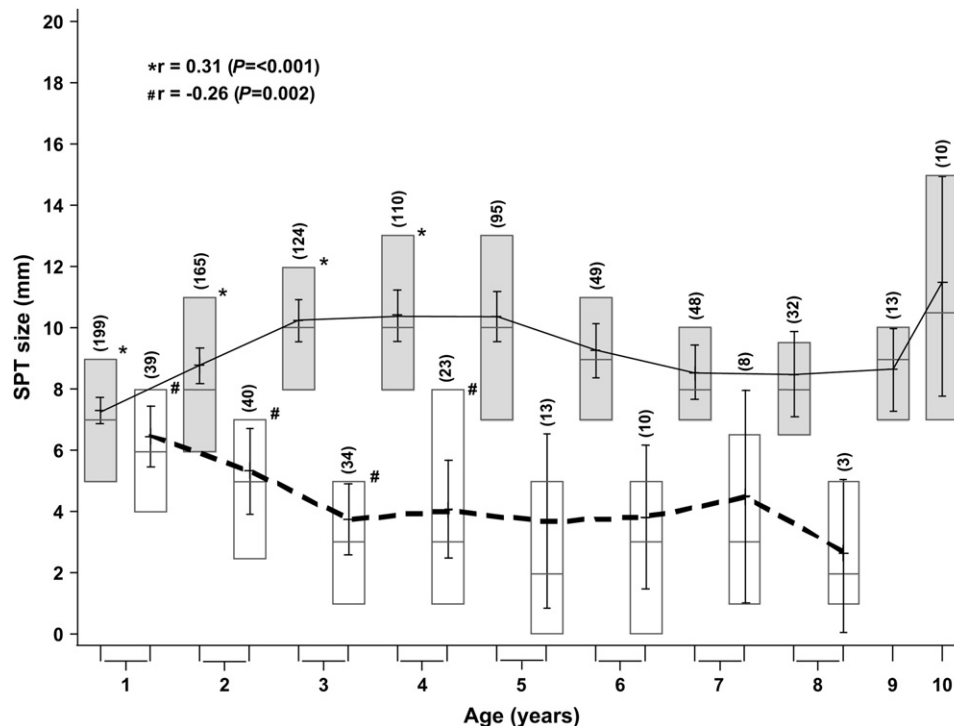


FIG 1. Evolution of SPT wheal size to peanut over the first 10 years of age. Shaded boxes represent the non-remitter group; open boxes represent the remitter group. The box represents the interquartile range, and the whiskers represent the 95% CIs of the means. SPT wheal diameters of nonremitters constantly increase (* $r = 0.31$, $P < .001$) and those of remitters decrease (# $r = -0.26$, $P = .002$) between the age of 1 and 4 years.

diameters of nonremitters increased ($r = 0.31$, $P < .001$), whereas that of remitters decreased ($r = -0.26$, $P = .002$) between the ages of 1 and 4 years. Such differences remained significant from 5 to 8 years of age.

Mode of presentation and outcome

The data were further analyzed according to whether the patients presented with an acute peanut reaction ($n = 93$) or not ($n = 174$, Table IV). Children presenting with a reaction were more likely to have been breast-fed for more than 4 months and less likely to have eczema or milk or egg allergy. However, at the preschool assessment, they were more likely to have eczema. There were 76 infants enrolled at less than 1 year of age. Of these, only 13 (17.1%) of 76 had an index reaction when compared with those enrolled at more than 1 year of age, of whom 80 (41.8%) of 191 had an index reaction ($P = .002$, χ^2 test). The children admitted to the study based on SPT criteria alone had the same rate of reactions to peanut after accidental ingestion compared with those who had an index clinical reaction (35/174 [20%] vs 19/93 [20%]).

There was no significant difference in the peanut remission rate, irrespective of the mode of presentation. However, there was a significant difference in mean SPT wheal diameter to peanut between the remitters and nonremitters (8.1 mm [SD, 3.3 mm] vs 7.2 mm [SD, 3.3 mm], $P = .026$) who had a peanut reaction before presentation.

Accidental reactions to peanut after diagnosis

Table III presents the frequency of accidental ingestion of peanut causing adverse reactions after enrollment: 54 (20.1%) of 267

children reported 59 episodes of immediate reactions (4.8 peanut accidents per 100 patient-years). Thirty-seven (63%) of these accidents occurred at home, with 13 (22%) requiring emergency department attendance (1.06 per 100 patient-years). Four patients self-administered adrenaline (EpiPen) before the arrival of paramedics (0.33 per 100 patient-years). The remitters had significantly fewer and less severe accidental reactions to peanut.

Analysis of predictors for remission of peanut allergy

Multivariate modeling by means of Cox regression analysis showed that SPTs of 6 mm or larger (hazard ratio, 2.16; 95% CI, 1.23-3.78; $P = .008$) and peanut-specific IgE antibody levels of 3 kUA/L or greater (hazard ratio, 2.74; 95% CI, 1.13-6.61; $P = .025$) before the age of 2 years were the only independent predictors of persistence of peanut allergy (Table V).

DISCUSSION

Both the size of the SPT wheal to peanut and the level of serum peanut-specific IgE before 2 years of age were independent predictors of clinical remission to peanut. However, age at diagnosis, mode of presentation, and severity of index reaction were not predictive of remission. SPT response to peanut extract of 6 mm or larger or peanut-specific IgE levels of greater than 3 KUA/L before 2 years of age halved the probability of tolerance development. The long-term prognosis for peanut allergy was also predicted by the directional change in SPT wheal size by 3 years of age. A 3 mm or greater increase of SPT wheal diameter

TABLE IV. Comparison of features at enrollment (median age, 14.1 months) and follow-up (median age, 4 years) according to whether patients had an index clinical reaction to peanut before enrollment

Enrollment variables	With index reaction, n = 93	Without index reaction, n = 174	P value
Male/female ratio	59/34	116/58	NS
Mean (range) duration of follow-up (mo)	61.7 (20-137)	58 (21-128)	NS
Exclusive breast-feeding ≥ 4 mo	77/93 (80%)	106/174 (60%)	.0004
Atopic eczema	44/93 (47%)	125/174 (72%)	<.0001
Egg allergy	42/93 (45%)	130/174 (75%)	<.0001
Milk allergy	20/93 (22%)	90/174 (52%)	<.0001

At 4-year-old assessment	With index reaction, n = 86	Without index reaction, n = 137	P value
Male/female ratio	54/32	89/48	NS
Median (range) age (mo)	49 (36-59)	46 (36-59)	NS
Δ Median SPT diameter 1-4 y (mm)	+2	+1	NS
Resolved peanut allergy	14/86 (16.3%)	26/137 (19.0%)	NS
Resolved egg allergy	30/44 (68.2%)	44/108 (40.7%)	.004
Resolved milk allergy	14/21 (66.6%)	50/70 (71.4%)	NS
Current atopic eczema	46/86 (53.5%)	41/137 (30.6%)	.0008
Current asthma	57/86 (66.2%)	79/137 (57.7%)	NS

P value of less than .05 is considered significant. NS, Not significant.

TABLE V. Predictors of persistence of peanut allergy according to multivariate analysis

Variable	Hazard ratio	95% CI	P value
SPT to peanut extract ≥ 6 mm before 2 y of age	2.16	1.23-3.79	.008
FEIA, peanut-specific IgE (SD) ≥ 3 kUA/L before 2 y of age	2.74	1.13-6.61	.025
Tree nut sensitization before 2 y of age	0.64	0.33-1.26	NS
Sesame sensitization before 2 y of age	0.44	0.71-0.30	NS
Age at diagnosis of peanut allergy <12 mo	1.58	0.78-3.20	NS
Egg allergy before 2 y of age	1.29	0.70-2.37	NS
Milk allergy before 2 y of age	1.43	0.81-2.53	NS
Inhalation allergen sensitization before 2 y of age	0.69	0.38-1.24	NS
Total IgE >100 U/L	0.74	0.38-1.45	NS

P value of less than .05 is considered significant. NS, Not significant.

between 1 and 4 years was strongly predictive of persisting peanut allergy, whereas decreasing levels were a good prognostic sign.

Although early tree nut, sesame, or both cosensitizations were associated with an increased likelihood of persistent peanut allergy, multivariate analysis failed to confirm that they were independent predictors, and they are therefore likely to be confounding factors. Other factors, including sex, total IgE levels, comorbidities with other atopic manifestations or food allergy, frequency of ingestion of soy formula in the first 2 years of life, and early inhalation allergen sensitization were not related to prognosis.

Resolution of peanut allergy was achieved in 21.4% of study participants by the age of 5 years and was similar to the remission rate reported by others.¹¹⁻¹³ Kaplan-Meier curves showed that the cumulative tolerance probability was 34.2% at 7 years of age, and in this cohort no further remissions occurred after that age. It is possible our selection of patients for oral peanut challenge based on SPT levels might have led us to underestimate the true rate of development of peanut tolerance. However, we have previously developed and validated 95th percentile PPVs for peanut allergy by using this study's skin prick testing methodology in a wide age range,^{14,15} and we could not ethically offer follow-up food

challenges to those children with greater than 95% PPVs at the conclusion of the study. In the future, correlation of peanut-specific IgE serum levels and SPT wheal size will be a useful adjunct for decisions regarding timing of food challenges now that clear 95% PPVs for both of these methods have been defined.¹⁷⁻¹⁹ We were unable to undertake this because peanut-specific IgE serum levels were not available on all study participants.

One limitation of this study is that not all patients underwent food challenges to peanut, and therefore some might have been only peanut sensitized rather than having true peanut allergy. Based on our previous work, we had identified 95% PPVs for peanut by means of formal food challenge in young children¹⁵ and subsequently validated these results further in infants and young children who had not been previously exposed to peanut.¹⁴ We therefore believe it would have been unethical to challenge all of these subjects because the majority would react.

In concurrence with other reports,^{11,20} 20% of our patients had clinical reactions after accidental peanut ingestion, although only 4% of the cohort required emergency department attendance, and 2% used self-administered adrenalin before paramedic attendance. This is despite clear guidelines to avoid all peanuts and tree nuts, including foods labeled "may contain traces of nuts."

Interestingly, the majority of reactions (35/54 [65%]) occurred in those children who had not presented with an index clinical reaction but who were given diagnoses after presentation with other food allergies or eczema, suggesting that parents were not fully convinced that their child had peanut allergy. Repeated accidental ingestions were unlikely occurrences because only 59 accidental ingestions were noted among 54 children, perhaps suggesting increased vigilance by parents after unexpected reactions.

An unexpected finding was the high rate of newly developed sesame seed and other tree nut allergies among children with peanut allergy despite recommendations to strictly avoid all tree nuts and seeds in addition to peanuts. Development of new-onset allergies to these foods despite strict avoidance suggests a mechanism of antigenic cross-reactivity leading to cross-sensitization.²¹ On the other hand, we found no evidence that the ingestion of soy milk, which contains shared IgE epitopes with Ara h 3,²² influenced the subsequent development of tolerance to peanut.

This study further validates the use of SPTs in clinical practice. Although the size of the SPT wheal does not predict the severity of reactions after ingestion of peanut,²³ in centers in which the 95% PPVs for SPTs have been validated against formal food challenges,^{24,25} the need for confirmatory but expensive and potentially dangerous peanut food challenges has been significantly reduced.

Novel recombinant peanut allergens under development for skin prick testing and further delineation of immunoreactive epitopes could further help identify those most likely to remit from those in whom peanut allergy is likely to persist.²⁶

In this large cohort of children based at a single tertiary pediatric allergy center, the most sensitive predictors of persistent peanut sensitization were serum peanut-specific IgE levels of greater than 3 kUA/L in children less than 2 years old and an increasing SPT wheal of greater than 3 mm between the ages of 1 and 4 years. These results will help to correctly identify children at high risk of persistent peanut allergy so that they can be appropriately targeted for novel therapeutic interventions.

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Clinical implications: Annual skin prick testing between the ages of 1 and 4 years is valuable in predicting those who will become peanut tolerant.

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