

The natural progression of peanut allergy: Resolution and the possibility of recurrence

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Background: It was once thought that peanut allergy is a lifelong problem. We previously reported that about 20% of children outgrow their peanut allergy and that more than 60% of patients with a peanut-IgE level of 5 or less passed an oral challenge. **Objective:** The goal of this study was to further describe the natural progression of peanut allergy by reviewing patients who have undergone oral peanut challenges since the previous study.

Methods: Patients with peanut-IgE levels of 5 or less were offered a peanut challenge. Those who passed were further evaluated by questionnaire to assess reintroduction of peanut into their diet and whether any recurrence has occurred.

Results: Eighty-four patients were evaluated, and 80 underwent complete analysis. Fifty-five percent with peanut-IgE levels of 5 or less and 63% with peanut-IgE levels of 2 or less passed challenges, compared to 61% and 67%, respectively, in our previous study. The 4 additional patients passed peanut challenges in this study after previously failing. Three patients with initial anaphylactic reactions and 2 patients with initial peanut-IgE levels greater than 70 passed their challenge. Follow-up of those who passed in both studies showed that the majority of patients reintroduced peanut into their diet, but that continued label reading, infrequent/limited ingestion, and aversion to peanut were all common in this population. Two patients had suspected subsequent reactions to peanut after passing their challenge.

Conclusions: Patients with a history of peanut allergy and peanut-IgE levels of 5 or less have at least a 50% chance of outgrowing their allergy. Recurrence of peanut allergy may occur but appears to be uncommon. (*J Allergy Clin Immunol* 2003;112:183-9.)

Key words: Peanut allergy, food challenge, recurrence, RAST, food hypersensitivity

Peanut allergy is common, with studies from the United States, the United Kingdom, and France estimating a prevalence of 0.4% in children and an overall prevalence

Abbreviations used

DBPCFC: Double-blind, placebo-controlled food challenge
FEIA: Fluorescent-enzyme immunoassay
kU_A/L: Kilounits of antibody per liter
PN-IgE: Peanut-specific IgE level
SPT: Skin prick test

of 0.5% to 1% in the general population.¹⁻³ There is evidence that the prevalence is rising, on the basis of a recent report from the Isle of Wight that showed a 2-fold increase in reported allergy, a 3-fold increase in peanut sensitization, and an overall estimate of peanut allergy of 1.5%.⁴ Consumption of peanut in Western countries may also be rising because of its use as a source of protein in health foods, the popularity of vegetarianism, and increased use of prepared foods. If we couple the rising prevalence and increased consumption with the facts that about 75% of children experience a reaction on their first known exposure,^{5,6} allergic reactions have the potential to be severe or even fatal,⁷ and accidental exposures are common,⁸ these numbers become even more significant.

We now know that peanut allergy is not always a lifelong problem on the basis of results from a recent study from our institutions⁹ as well as reports from other institutions.¹⁰⁻¹² In our study we found that about 20% of children outgrew their peanut allergy. Although this is reassuring for certain patients and families, a new concern has arisen for this limited group of patients with resolved peanut allergy: the possibility of a recurrence of their allergy after reintroduction of peanut into the diet. There have now been 3 reported cases of children who passed a peanut challenge but subsequently had an allergic reaction to peanut.¹³

In this study we sought to further describe the natural progression of peanut allergy by reviewing patients who have undergone oral peanut challenge since our previous study.⁹ We characterized their initial reactions and history of other food allergies and atopic diseases to determine any factors that might predict the tendency to outgrow peanut allergy. In addition, we contacted those families whose children passed their peanut challenge either in this study or in our previous study⁹ to determine whether peanut was reintroduced into the diet, how frequently it was consumed, and whether there was any evidence of a recurrence of their peanut allergy.

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METHODS

Study population

Patients diagnosed with peanut allergy who had undergone oral peanut challenge from April 2000 to November 2002 were identified from the Johns Hopkins Pediatric Allergy Clinic, the Arkansas Children's Hospital Pediatric Allergy Clinic, and the private practice of one of the investigators (R.A.W.). Patients were diagnosed to have peanut allergy if they met the following criteria: a history of an acute reaction after ingesting peanut and a positive skin prick test (SPT) result, peanut-specific IgE (PN-IgE) level, or challenge, or in some cases no history of peanut ingestion but a positive SPT result or PN-IgE level. All patients were 4 years or older and had PN-IgE levels less than 5 kilounits of antibody per liter (kU_A/L) at the time of challenge. Peanut challenges, either open or double-blind, placebo-controlled food challenges (DBPCFCs), were performed as part of the routine clinical care of these patients or as part of ongoing research studies. Patients who had passed peanut challenges, both in this study and in the previous study at our institutions,⁹ were further evaluated by completing a telephone questionnaire. The study protocol was approved by the investigational review boards of the Johns Hopkins University School of Medicine and the University of Arkansas for Medical Sciences.

Chart review and questionnaire

Patient charts were reviewed to extract details about the initial presentation, including age of first reaction, extent of symptoms (in those patients who had consumed peanut), the organ systems involved, including the skin (urticaria, edema, erythema), gastrointestinal tract (abdominal pain, vomiting, diarrhea), and respiratory tract (difficulty breathing, wheezing, coughing, throat tightness, nasal congestion). Anaphylaxis was defined as a reaction involving all 3 organ systems. Information about the presence of other food allergies, whether still present or outgrown, and the presence of other atopic diseases was obtained. Finally, all available SPT results, PN-IgE levels, and details of the challenges were recorded.

Follow-up letters were sent to all patients who passed peanut challenges in this study and our previous study.⁹ The letters provided details on the purpose of the follow-up and requested consent to allow telephone contact to complete the questionnaire. The questionnaire gathered the following information: whether the families still read all food labels looking for peanut, whether the patients had eaten peanut products since passing the challenge, what types of food they ate, how frequently they ate them, and whether there was any evidence of a recurrence of their peanut allergy.

Laboratory studies

SPTs, CAP-RAST tests (Pharmacia, Uppsala, Sweden), and peanut challenges were performed as previously described.⁹

Statistical analysis

Patients challenged were divided into those who passed and those who failed. Negative PN-IgE levels, less than $0.35 kU_A/L$, were arbitrarily assigned a level of 0.1 for the purpose of analysis. PN-IgE levels were compared by use of the Mann-Whitney *U* test. The frequencies of other atopic diseases and other food allergies in these groups were compared by use of the chi-square test.

RESULTS

Peanut challenge results

A total of 84 patients with peanut allergy, 73 from Johns Hopkins Hospital and 11 from Arkansas Children's Hos-

pital, underwent challenges during the study period, of which 78 were open challenges and 6 were DBPCFCs. Four of the 84 patients were unique because they had undergone multiple peanut challenges; therefore they were excluded from the complete analysis. These 4 patients will be described separately at the end of this section, and the following results refer to the other 80 patients.

The study population, described in Table I, included 50 male (63%) and 30 (37%) female patients. Age at initial diagnosis ranged from 8 months to 5 years (median, 1.3 years). The initial diagnosis was made on the basis of a history of an acute reaction to peanut in 60 patients (75%), 53 (88%) of whom in addition had a positive SPT result or PN-IgE level at the time of diagnosis, whereas the other 7 patients in this group did not have a confirmatory SPT or PN-IgE level performed. The remaining group of 20 patients had never ingested peanut but were diagnosed by a positive SPT result or PN-IgE level, including 5 with a positive SPT result, 13 with a positive PN-IgE level, and 2 with both. PN-IgE levels at the time of diagnosis in this latter group ranged from 0.5 to $82.2 kU_A/L$ (median, $2.7 kU_A/L$).

As seen in Table I, 44 patients (55%), who ranged in age from 4 to 10.9 years at the time of challenge (median, 5.9 years) and 4.7 to 11.8 years at the time of chart review (median, 6.3 years), passed challenges. The 36 patients who failed had similar ages at challenge and at chart review, 4 to 14.2 years (median, 5.9 years) and 4.5 to 15 years (median, 6.2 years), respectively. Thirty-two of the 60 patients (53%) diagnosed on the basis of a history of an acute reaction passed their challenge, and 12 of the 20 (60%) diagnosed by a positive SPT result or PN-IgE level passed their challenge. PN-IgE levels at challenge for those who passed, which ranged from less than 0.35 to $4.9 kU_A/L$ (median, less than 0.35), were significantly lower than the PN-IgE levels of patients who failed ($P < .02$), which ranged from less than 0.35 to $5 kU_A/L$ (median, 1.85) (Fig 1).

The percentages of patients who passed or failed were determined at different cutoffs of PN-IgE levels at challenge (Table II). Thirty-six of 57 patients (63%) with PN-IgE levels of $2 kU_A/L$ or less and 22 of 30 patients (73%) with negative PN-IgE levels passed challenges. Eight of 23 patients (35%) with PN-IgE levels between 2 and $5 kU_A/L$ and 14 of 27 patients (52%) with PN-IgE levels between 0.35 and $2 kU_A/L$ passed challenges. Children with PN-IgE levels of $2 kU_A/L$ or less were significantly more likely to pass than those with PN-IgE levels between 2 and 5 ($P < .003$).

Initial PN-IgE levels at diagnosis were available in 21 of the 44 who passed challenges, and they ranged from less than 0.35 to $82.2 kU_A/L$ (median, $1.1 kU_A/L$) (Fig 2). These were not significantly different from the initial PN-IgE levels available in the 13 of 36 patients who failed challenges (range, < 0.35 to $23.9 kU_A/L$; median, $3.0 kU_A/L$) ($P = .12$). Two of the patients who passed had initial PN-IgE levels greater than $70 kU_A/L$, whereas only 1 patient who failed had an initial PN-IgE level greater than $20 kU_A/L$.

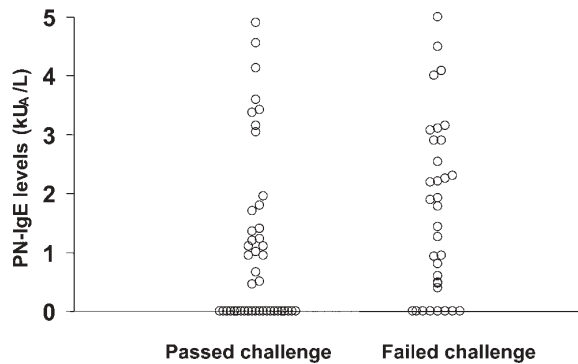


FIG 1. PN-IgE levels at challenge in patients who passed challenges (n = 44; range, < 0.35 to 4.9 kU_A/L; median, < 0.35 kU_A/L) and failed challenges (n = 36; range, < 0.35 to 5 kU_A/L; median, 1.85 kU_A/L).

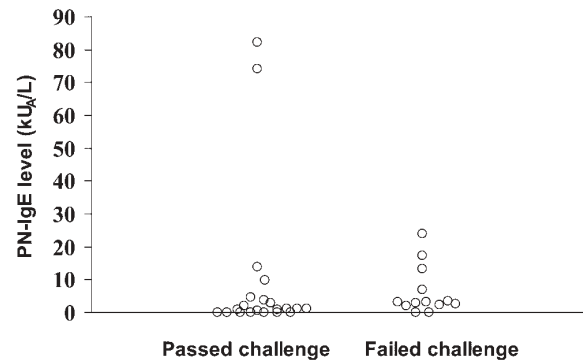


FIG 2. Initial PN-IgE levels at diagnosis in patients who passed challenges (n = 21; range, < 0.35 to 82.2 kU_A/L; median, 1.1 kU_A/L) and failed challenges (n = 13; range, < 0.35 to 23.9 kU_A/L; median, 3.0 kU_A/L).

TABLE I. Patient characteristics

	Passed challenge (n = 44) (55%)	Failed challenge (n = 36) (45%)	Total (n = 80)
Male (%)	26 (59)	24 (67)	50 (63%)
Female (%)	18 (41)	12 (33)	30 (37%)
Age at diagnosis (y)			
Range	0.8-5	0.7-2.5	0.7-5
Median	1.3	1.3	1.3
PN-IgE at diagnosis (kU _A /L)	(n = 21)	(n = 13)	(n = 34)
Range	< 0.35-82.2	< 0.35-23.9	< 0.35-82.2
Median	1.1	3.0	2.2
No. diagnosed by history (%)	32 (53)	28 (47)	60 (75)
No. diagnosed by SPT or RAST (%)	12 (60)	8 (40)	20 (25)
Age at challenge (y)			
Range	4-10.9	4-14.2	4-14.2
Median	5.9	5.9	5.9
PN-IgE at challenge (kU _A /L)			
Range	< 0.35-4.9	< 0.35-5.0	< 0.35-5.0
Median	< 0.35	1.85	0.95
Current age (y)			
Range	4.7-11.8	4.5-15	4.5-15
Median	6.3	6.2	6.3

Initial reactions to peanut are described in Table III. Of the 47 patients with only one system involvement on initial reaction (46 skin and 1 gastrointestinal), 26 patients (55%), all with skin only, passed peanut challenges. Three of 9 patients with 2-system involvement passed the challenge, and 3 of 4 patients with an initial anaphylactic reaction outgrew their allergy. The severity of initial reactions, defined on the basis of the number of systems involved, was not predictive of peanut challenge outcome.

Associated atopic disorders, including the presence of other past or present food allergies, are described in Table IV. Sixty-six patients (83%) had at least 1 additional atopic disorder other than food allergy, including asthma, allergic rhinitis, or atopic dermatitis. The different types and numbers of atopic disorders were not predictive of challenge outcome. Forty-five patients (56%) had at least 1 food allergy other than peanut, and 27 (60%) of these passed a peanut challenge. Egg, milk, and tree nut allergy were the 3 most common other food allergies at 36%, 30%, and 20%, respectively. Fifteen

TABLE II. PN-IgE levels and pass/fail rates

PN-IgE levels at challenge (kUa/L)	Passed challenge (%)	Failed challenge (%)
≤5	44 (55)	36 (45)
≤2	36 (63)	21 (37)
<0.35	22 (73)	8 (27)
2.01-5	8 (35)	15 (65)
0.35-2	14 (52)	13 (48)

patients (19%) had 1 additional food allergy with 8 (53%) passing a challenge, and 19 patients (24%) had 2 additional food allergies with 14 (74%) passing a challenge. There were 11 patients who had 3 or more other food allergies: 5 patients with 3 food allergies, 1 patient with 4 food allergies, 2 patients with 5 food allergies, and 3 patients with 6 food allergies. Five of these 11 patients (45%) passed their peanut challenge. Patients with a history of food allergy other than peanut in the past or at the

TABLE III. Characteristics of initial reactions

	Passed challenge (n = 32) (%)	Failed challenge (n = 28) (%)	Total (n = 60) (%)
Skin only	26 (57)	20 (43)	46 (77)
Gastrointestinal only	0	1 (100)	1 (2)
Respiratory only	0	0	0
Skin and gastrointestinal	2 (40)	3 (60)	5 (8)
Skin and respiratory	1 (25)	3 (75)	4 (7)
Gastrointestinal and respiratory	0	0	0
All 3 systems	3 (75)	1 (25)	4 (7)

TABLE IV. Associated atopic disorders

	Passed challenge (%)	Failed challenge (%)	Total (%)
Asthma	23 (59)	16 (41)	39 (49)
Allergic rhinitis	19 (56)	15 (44)	34 (43)
Atopic dermatitis	28 (57)	21 (43)	49 (61)
Asthma and allergic rhinitis	2 (67)	1 (33)	3 (4)
Asthma and atopic dermatitis	6 (55)	5 (45)	11 (14)
Allergic rhinitis and atopic dermatitis	4 (50)	4 (50)	8 (10)
Asthma, allergic rhinitis, and atopic dermatitis	11 (65)	6 (35)	17 (21)
History of other food allergy (past or present)	27 (60)	18 (40)	45 (56)
No history of other food allergy	17 (49)	18 (51)	35 (44)
Current other food allergies	16 (70)	7 (30)	23 (29)
Outgrown food allergies	18 (55)	15 (45)	33 (41)
No atopic disorder except food allergy (other than peanut)	3 (75)	1 (25)	4 (5)
No other atopic disorder	8 (57)	6 (43)	14 (18)
No atopic disorder and no other food allergy	5 (50)	5 (50)	10 (13)

time of challenge were not significantly more likely to pass a challenge than those patients with no history of other food allergy ($P = .31$).

Thirty-three patients (41%) had outgrown at least 1 other food allergy, with 6 food allergies the most outgrown, and 18 (55%) passed a food challenge. Twenty-three patients (29%) at the time of challenge currently had at least 1 additional food allergy, with 5 as the highest number of additional allergies, and 16 patients (69%) of these passed a challenge. Patients who had outgrown other food allergies at the time of challenge were not significantly more likely to pass than those who currently had other food allergies at challenge ($P = .26$).

There were 5 patients who underwent a challenge in this study who had met challenge criteria in the previous study,⁹ but who had declined to be challenged at that time. All were male with a median age of 6 years at the time of the prior study and 7.8 years at the time of their challenge. Two patients passed their challenge with PN-IgE levels of less than 0.35 and 0.5 kU_A/L, which had dropped from levels of 2.5 and 8.7 kU_A/L, respectively, at the time of the prior study. Of the 3 who failed, 2 had PN-IgE levels greater than 5 kU_A/L at the time of the prior study (7.2 and 6.3 kU_A/L), which had dropped to 2.21 and 2.91 kU_A/L, respectively, at challenge; the third patient's PN-IgE level fell from 0.52 to less than 0.35 kU_A/L in the interim between studies.

The final 4 children are unique in that they had multiple challenges. Two, both male, had failed their initial challenge in the previous study at ages 4.1 and 4.8 years

and subsequently passed a challenge in this study at ages 6.5 and 7.1 years, respectively. The other 2, both female, failed initial challenge in this study at ages 3.2 and 4.8 years but passed a subsequent challenge during this study period at ages 5.2 and 6.7 years, respectively. Three patients were diagnosed on the basis of history of a reaction, and all 3 had only skin involvement at that time. One patient, initially challenged at age 3.2 years, was diagnosed by skin testing and had never eaten peanut before the initial challenge. Three patients had negative PN-IgE levels at the time of both challenges, and the other patient's levels dropped from 2.68 kU_A/L at the first challenge to 1.7 kU_A/L at the subsequent challenge. The median time between challenges was 2.2 years.

Questionnaire results

A total of 96 patients from the 2 studies passed challenges, 48 from our original study and 48 from this study, including the 4 who underwent multiple challenges. Nine patients were not contacted because the time between their challenges and the follow-up questionnaire was less than 3 months, the minimal amount of time deemed necessary by us to establish a pattern of peanut ingestion. Eighty-seven letters were sent to obtain consent for the questionnaire, and 64 families completed the survey (74% of the 87 eligible and 67% of the total 96 who passed). The remaining 23 families either declined to participate or were unable to be reached because of change of address or phone number. The results of the questionnaire are described in Table V.

TABLE V. Follow-up questionnaire results

A. Follow-up and age						
	<i>Age at food challenge</i>	<i>Age at follow-up</i>	<i>Interval time of follow-up</i>			
Range (y)	4-17.6	4.7-20.3	0.3-5.9			
Median (y)	5.6	7.5	1.6			
B. Follow-up and label reading		<i>Yes</i>	<i>No</i>			
No. who still read labels for peanut (%)		22* (34)	42 (66)			
Age at follow-up (y)						
Range		4.7-20.3	4.7-16.8			
Median		7.1	7.8			
Interval time of follow-up (y)						
Range		0.3-5.9	0.3-5.5			
Median		0.8	2.4			
C. Follow-up and eating frequency						
Total: n = 64		<i>Rarely but now avoid</i>				
	<i>Never</i>	<i>Rarely</i>		<i>Occasionally</i>	<i>Frequently</i>	<i>Regularly</i>
No. who eat	2	22	1	21	12	6
Percent	3	34	2	33	19	9

Rarely, Several times a year; *Rarely but now avoid*, because of possible recurrence; *Occasionally*, approximately once a month; *Frequently*, approximately once a week; *Regularly*, almost daily.

*Includes 5 patients who read labels primarily because of tree nut allergy.

The median age at food challenge was 5.6 years (range, 4 to 17.6 years), and the median age at telephone contact was 7.5 years (range, 4.7 to 20.3 years). The median age between passing the challenge and telephone contact was 1.6 years (range, 0.3 to 5.9 years). Twenty-two patients (34%) still read labels for peanut products, 5 of whom continued to read labels primarily because of tree nut allergy. Sixty-two patients (97%) had eaten peanut products, and the remaining 2 did not eat peanut because of continued concern about a possible reaction. Twenty-two patients (34%) rarely ate it (several times/year), 1 patient (2%) rarely ate it but now avoids it because of a possible recurrence, 21 patients (33%) ate it occasionally (about once a month), 12 patients (19%) ate it frequently (about once/week), and 6 patients (9%) ate it on a regular basis (almost daily).

There were 2 patients, both female, who rarely ate peanut after passing their challenge who subsequently had a possible recurrence of their peanut allergy. Patient 1 had an initial anaphylactic reaction at age 2 years. The initial PN-IgE level was negative, and it remained negative at the time of challenge. She had asthma, allergic rhinitis, and atopic dermatitis and was allergic to fish at the time of challenge. She passed a peanut challenge at age 9.6 years, and the telephone questionnaire was done at age 10.5 years. Nine months before telephone contact, she ate 2 handfuls of shelled peanuts and developed urticaria. She was reexposed to peanut in the form of peanut butter and a peanut candy bar about 7 and 9 months later without any reaction. A repeat PN-IgE level was again negative.

Patient 2 had an initial reaction at age 2 years involving both the skin and gastrointestinal systems. The initial PN-IgE level was 1.21 kU_A/L, but it was negative at the time of challenge. She had asthma, allergic rhinitis, and atopic dermatitis and was allergic to tree nuts at the time

of challenge. The peanut challenge was passed at age 5.1 years, and the telephone survey was done at age 6.3 years. She never liked the taste of peanuts, but about 15 months after passing her challenge she ate a peanut candy and within 5 minutes had vomiting. A repeat trial several days later with the same food caused the same reaction. A repeat PN-IgE level increased to 1.8 kU_A/L.

DISCUSSION

This study confirms that a subset of children with peanut allergy can outgrow their allergy over time. Fifty-five percent of children with PN-IgE levels of 5 kU_A/L or less, 63% with PN-IgE levels of 2 kU_A/L or less, and 73% with negative PN-IgE levels passed an oral challenge, compared to 61%, 67%, and 73%, respectively, in our previous study.⁹ We cannot determine the overall rate of outgrowing peanut allergy in this study because we only challenged children with PN-IgE levels less than 5 kU_A/L. However, if we add the 2 patients who refused a challenge in the prior study but passed their challenge in this study and the 2 patients who originally failed a challenge in the previous study⁹ but passed their challenge in this study, the overall rate of outgrowing peanut allergy from the prior study would increase to 23.3%.

This study confirms the value of performing oral challenges in select children with peanut allergy, especially when considering the tremendous burden that peanut allergy causes for children and their families. Although we continue to believe that PN-IgE levels are the best guide to determine which patients merit challenge, it is important to emphasize the point that PN-IgE levels remain by no means foolproof in determining who will pass or fail, as seen by the 8 patients who failed despite having negative PN-IgE levels at the time of

challenge. Furthermore, all peanut challenges should be done in a controlled environment with experienced clinicians because the potential for severe reactions exists at any PN-IgE level.

We would still recommend that these challenges not be performed until at least age 4 years and that a PN-IgE level less than 5 kU_A/L be used as the cutoff for challenge for most children. However, on the basis of the current data, a cutoff of less than 2 kU_A/L would be more appropriate in clinical practice. Although 55% of children with a level less than 5 kU_A/L passed their challenge, it should be recognized that the chance of passing a challenge was only 35% with levels between 2 and 5 kU_A/L and did not exceed 50% until levels were less than 2 kU_A/L. This study also demonstrates that a subset of children merit rechallenge after a failure, on the basis of the 4 patients who passed their second challenge. This should be considered particularly for younger children who had mild reactions on their initial challenge.

There are several limitations to the current study that should be noted. First, the patients in this study might not be typical of all patients with peanut allergy because they were referred to tertiary care centers. Second, DBPCFCs are still considered the gold standard for food challenges, but more than 90% of our challenges were performed as open challenges. Therefore, it is possible that some of the positive results could have been the result of physiologic stress rather than true ongoing allergy, thus underestimating the number who would have passed. Finally, these numbers may be an overestimate because we included those children who had never eaten peanut but avoided it because they had a positive SPT result or PN-IgE level. It should be noted, however, that 8 of 20 children who had never eaten peanut still failed their challenge, and the pass rates of those diagnosed by history (53%) were similar to the pass rates of those diagnosed by a positive SPT result or PN-IgE level (60%).

The PN-IgE levels at the time of challenge in this study were significantly lower in the group who passed than in the group who failed. Initial PN-IgE levels were only available on 34 of the 80 patients and were not significantly different between the 2 groups. They tended to be low in both groups, but it should be noted that there were 2 children who passed their challenge who had high initial levels of 74.2 and 82.2 kU_A/L, demonstrating that even some patients with very high initial PN-IgE levels can eventually outgrow their allergy.

Initial peanut reactions were not predictive of future challenge outcome as they had been in our previous study in which patients who outgrew their allergies were significantly more likely to have had initial reactions involving the skin only compared to those with ongoing peanut allergy.⁹ In addition, unlike the previous study in which patients with ongoing peanut allergy were significantly more likely to have had an initial reaction involving 3 systems,⁹ 3 of 4 patients in this study who had anaphylactic reactions outgrew their allergy. These results are in contrast to a previous report by Spergel et al¹² in which no patients out of 5 with initial anaphylaxis passed a challenge.

There have been very few studies that address subsequent peanut consumption in patients who have outgrown their peanut allergy. Hourihane et al¹⁰ were able to contact 14 patients up to 2 years later after passing a challenge and found that 7 patients ate peanuts without problems, 5 had eaten peanuts but did not like them, and only 2 had never eaten peanuts. They concluded that although no exposures to peanut in resolvers had resulted in allergic reactions, aversion and ongoing avoidance were common. Busse et al¹⁴ reported on 21 children who had resolved peanut allergy after a mean follow-up period of 15 months. Ten routinely ate peanut, 5 occasionally ate small amounts but disliked it, 1 avoided completely for dislike, and 2 never reintroduced it.

In this study we found that 97% of patients contacted had eaten peanut after passing their challenges, but about 70% ate peanuts at most about once a month, and only 30% ate peanuts on a somewhat regular basis. Even if we exclude the patients who continue to read labels primarily because of tree nut allergy, there is still a substantial portion of families who still read all labels. The most common reasons reported for this were that parents (and some older patients) were still wary of a possible reaction, or they wanted to limit the amount of peanut that their children ate, thinking that a larger amount might cause a severe reaction. It should be noted, however, that the median amount of time between the challenge date and the date of the telephone questionnaire for the group of families who still read labels was 0.8 years versus 2.4 years for the group who no longer read labels. Therefore, ongoing label reading might be a matter of habit that diminishes over time.

The final purpose of this study was to assess for any possible recurrences of peanut allergy. Busse et al^{13,14} recently reported on 3 patients who had a recurrence of their allergy, yielding a recurrence rate of 14% in their population at the time of report. All 3 patients ate peanut infrequently in small amounts, had negative PN-IgE levels at the time of challenge, and had an increase in their PN-IgE levels (0.41 kU_A/L, 1.2 kU_A/L, and 16.6 kU_A/L) on repeat testing after their recurrence. The authors speculated that resensitization might have occurred because these patients ingested only small amounts of peanut intermittently, rather than ingesting small amounts frequently or larger amounts intermittently that might better sustain tolerance. They recommended that patients with resolved peanut allergy should continue to carry epinephrine for at least 1 to 2 years until they tolerate eating regular amounts with relative consistency.

In this study we found 2 possible cases of recurrence in the 64 patients with resolved peanut allergy whom we were able to contact. However, neither of these is definite in that one with a known aversion to the taste of peanut only had vomiting, and the second has now tolerated peanuts on 2 occasions after her suspected reaction. At worst, this yields a current recurrence rate of 3% if they are truly resensitized, although we cannot be fully reassured without doing further study, especially because so many patients fit into the group who eat only infrequent,

small amounts and therefore might still be at risk for recurrence. The best approach to this dilemma is far from clear, and although there are no scientifically proven recommendations, it might make most sense to recommend that peanut be eaten with some regularity after challenge. We would also recommend that patients continue to keep epinephrine on hand until they have proved that they tolerate peanut during a 1- to 2-year period. For those patients who continue to avoid peanut or are only exposed infrequently, it would be prudent to keep epinephrine on hand indefinitely and to consider intermittent reevaluation.

We conclude that a subset of children do indeed outgrow their peanut allergy, even some who had initial anaphylactic reactions or high initial PN-IgE levels and select patients who have failed a previous challenge. The severity of initial reactions, the presence or absence of other food allergies or other atopic disorders, and whether other food allergies had been outgrown were all not predictive of peanut challenge outcome. Although we have confirmed that children 4 years or older with PN-IgE levels less than 5 kU_A/L have an overall 50% chance of passing a peanut challenge and thus might merit challenge in a properly supervised setting, we would recommend that a PN-IgE cutoff of 2 kU_A/L might be more appropriate for clinical practice to ensure a higher chance of success.

We acknowledge the fact that the recurrence of peanut allergy is a reality that allergists and families must now face and that the limited consumption of peanut after outgrowing the allergy might increase this risk. Although the exact mechanisms causing this recurrence and what to do about it are not completely clear at this time, answers should be forthcoming with ongoing study of this unique population of patients.

REFERENCES

1. Sicherer SH, Muñoz-Furlong A, Burks WA, Sampson HA. Prevalence of peanut and tree nut allergy in the US determined by a random digit dial telephone survey. *J Allergy Clin Immunol* 1999;103:559-62.
2. Emmett SE, Angus FJ, Fry JS, Lee PN. Perceived prevalence of peanut allergy in Great Britain and its association with other atopic conditions and with peanut in other household members. *Allergy* 1999;54:380-5.
3. Kanny G, Moneret-Vautrin DA, Flabbee J, Beaudouin E, Morisset M, Thevenin F. Population study of food allergy in France. *J Allergy Clin Immunol* 2001;108:133-40.
4. Grundy J, Matthews S, Bateman B, Dean T, Arshad SH. Rising prevalence of allergy to peanut in children: data from 2 sequential cohorts. *J Allergy Clin Immunol* 2002;110:784-9.
5. Sicherer SH, Furlong TJ, Muñoz-Furlong A, Burks AW, Sampson HA. A voluntary registry for peanut and tree nut allergy: characteristics of the first 5149 registrants. *J Allergy Clin Immunol* 2001;108:128-32.
6. Hourihane JO'B, Dean TP, Warner JO. Peanut allergy in relation to heredity, maternal diet, and other atopic diseases: results of a questionnaire survey, skin prick testing, and food challenges. *BMJ* 1996;313:518-21.
7. Bock SA, Muñoz-Furlong A, Sampson HA. Fatalities due to anaphylactic reactions to foods. *J Allergy Clin Immunol* 2001;107:191-3.
8. Sicherer SH, Burks WA, Sampson HA. Clinical features of acute allergic reactions to peanut and tree nuts in children. *Pediatrics* 1998;102:e6.
9. 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.
10. Hourihane JO'B, Roberts SA, Warner JO. Resolution of peanut allergy: case-control study. *BMJ* 1998;316:1271-5.
11. Vander Leek TK, Liu AH, Stefanski K, Blacker B, Bock SA. The natural history of peanut allergy in young children and its association with serum peanut-specific IgE. *J Pediatr* 2000;137:749-55.
12. Spergel JM, Beausoleil JL, Pawlowski NA. Resolution of childhood peanut allergy. *Ann Allergy Asthma Immunol* 2000;85:473-6.
13. Busse PJ, Nowak-Węgrzyn AH, Noone SA, Sampson HA, Sicherer SH. Recurrent peanut allergy (correspondence). *N Engl J Med* 2002;347:1535-6.
14. Busse PJ, Noone SA, Nowak-Węgrzyn AH, Sampson HA, Sicherer SH. Recurrence of peanut allergy (abstract). *J Allergy Clin Immunol* 2002;109:S92.

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