

(1:1000, 0.3 cc). He had a 50% improvement in angioedema within 15 minutes. He received a second dose of IM epinephrine (1:1000, 0.3 cc) 4 hours later with complete resolution of oropharyngeal angioedema and successful extubation by the following morning.

Anaphylaxis may be uniphasic, biphasic (an acute episode that resolves with symptoms recurring 4-8 hours later), or protracted in nature.³ Protracted anaphylaxis despite treatment has been reported to last up to 3 weeks.⁴ In 2 series of patients with anaphylaxis, protracted anaphylaxis was seen in 23% (3 of 13) of children with food allergy⁴ and 28% (5 of 25) of adults with food or drug allergy.³

The recommended dosing of aqueous epinephrine for the treatment of anaphylaxis is 0.01 mg/kg up to 0.5 mg IM every 5-15 minutes as necessary.¹ In the case of patient 1, epinephrine was withheld during his first episode of anaphylaxis for over 2 weeks due to concern over his substantial cardiac risk factors. It is possible that the delay in administration of epinephrine contributed to his protracted laryngeal edema. Sampson et al⁴ showed that food-related anaphylaxis not treated with epinephrine before onset of severe symptoms was associated with increased mortality. In addition, a retrospective study in children showed that the median time to initial dose of subcutaneous epinephrine was higher in patients who developed biphasic anaphylaxis compared with those who developed uniphasic anaphylaxis (190 minutes vs 48 minutes).⁵ The possibility of the delay in epinephrine administration to patient 1 contributing to his first episode of protracted anaphylaxis is made less likely by his second episode, in which he developed protracted anaphylaxis despite receiving epinephrine acutely. Similarly, patient 2 had a protracted course despite an initial dose of IM epinephrine and a single dose of nebulized epinephrine.

Physician reluctance to use epinephrine in patients with significant cardiac risk factors is perhaps reinforced by a recent case report that details a patient without prior cardiac disease who developed arrhythmia and probable coronary artery vasospasm after treatment with IV epinephrine for postoperative anaphylaxis.⁶ If significant cardiac risk factors exist (as in both our patients), proper precautions should be taken and careful thought given prior to administration of epinephrine for the treatment of anaphylaxis. One could consider a lower than maximum dose of epinephrine initially to observe for arrhythmia and response, followed by repeated dosing as clinically indicated. We believe that the existence of significant cardiac risk factors should not preclude the appropriate treatment of anaphylaxis. In other words, cardiac disease should not be considered as an absolute contraindication for the use of epinephrine in treatment of anaphylaxis. Moreover, these 2 patients demonstrate that epinephrine remains the treatment of choice for anaphylaxis, be it in the acute or protracted phase.

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The natural history of peanut allergy: Extending our knowledge beyond childhood

To the Editor:

Although food allergy is a common problem in childhood, little information is available on the natural history of food allergy in adults. In clinical practice adults are typically advised to practice strict avoidance because food allergy is usually considered to be a lifelong condition. We characterized teenagers and adults with peanut allergy to gain insight into the natural history of peanut allergy beyond childhood. We chose peanut allergy because it is a common and often severe food allergy that persists into adulthood in a majority of patients.

We recruited subjects with peanut allergy 13 years and older and obtained a detailed clinical history. Prior reaction severity was graded as mild, moderate, or severe according to Perry et al.¹ Skin prick tests (SPTs) were performed with a Greer pick (Greer Laboratories, Lenoir, NC) to peanut, tree nuts (almond, cashew, hazelnut, pecan, and walnut), and tree and grass pollen mixes, as well as positive and negative controls. Mean wheal size was measured after 15 minutes. Peanut-specific IgE (pn-IgE) levels were measured for all subjects by using the ImmunoCap System FEIA (Phadia, Uppsala, Sweden). A double-blind, placebo-controlled food challenge (DBPCFC)² to peanut was offered to subjects with a pn-IgE level of less than 10 kU/L who had not had a convincing peanut reaction in the last year by using a cumulative dose of 8 g of peanut protein disguised in either chocolate or ground turkey. The study was approved by the Investigational Review Board of the Johns Hopkins University School of Medicine.

Subjects were divided into early- and late-onset peanut allergy groups based on clinical history. Subjects with early-onset peanut allergy had a history of reacting to peanut with their first few exposures to peanut products. Subjects with late-onset allergy had their first reaction at least 5 years after their first peanut exposure and had tolerated multiple (daily or weekly) exposures to peanut products before their first reaction. The diagnosis of peanut allergy was initially made in all subjects based on reported allergic symptoms on peanut ingestion, with the exception of 2 subjects (1 in the early-onset group and 1 in the late-onset group) who were initially given diagnoses on the basis of only a positive SPT response. The Mann-Whitney *U* test and χ^2 test were used to compare these groups.

Twenty-five subjects with early-onset and 10 with late-onset peanut allergy were identified (Table I). The median age at peanut allergy diagnosis was 3 years in the early-onset group and 25 years in the late-onset group. The subjects in the early-onset group had significantly larger peanut SPT wheal sizes (median, 5.3 vs 2.9 mm; $P = .03$), had higher pn-IgE levels (median, 2.5 vs 0.4 kU/L; $P = .05$), and were more likely to report a history of a severe reaction (92% vs 50%, $P < .01$) compared with the late-onset subjects. Concomitant tree nut allergy was similar between groups.

Of the early-onset group, 12 met the criteria for a DBPCFC, of whom 8 underwent a DBPCFC and 4 declined. Five of the 8 passed their challenges. Of the late-onset group, 5 met the criteria for and underwent a DBPCFC. Three of the 5 passed their challenges (Table II).

This study has therefore characterized a cohort of teens and adults with peanut allergy, SPT response, pn-IgE level, and, where appropriate, DBPCFC result. Subjects were divided on the basis of clinical history into early-onset and late-onset allergy groups according to when their allergy developed. The early-onset group had significantly more severe symptoms on peanut ingestion, larger

peanut SPT responses, and higher pn-IgE levels compared with the late-onset group.

Of the subjects with early-onset peanut allergy who underwent a peanut challenge, 4 of them passed their challenges. None had a reaction since their teenage years, and therefore we cannot be confident that any truly lost their allergy as adults. However, this suggests that food challenges should be considered into adulthood in the setting of a low or negative pn-IgE level with no recent reactions.

The results of SPTs and food-specific IgE measurements are often used to decide when to offer a patient a food challenge. We identified 7 subjects with peanut allergy (4 in the early-onset group and 3 in the late-onset group) with undetectable (<0.35 kU/L) pn-IgE levels. Three of the 7 failed a food challenge (Table II), and the remaining 4 were not challenged because they reported recent reactions. Two of the 7 had a negative SPT response as well. This is consistent with results from a pediatric population in which 24% with a negative pn-IgE result failed a food challenge.³ However, the relationship between IgE and clinical reactivity in adults does warrant further study.

We also identified individuals who had peanut allergy after being able to tolerate peanut products on a regular basis for years. Their pn-IgE levels were generally less than those in the early-onset group, and they were less likely to report severe reactions compared with the early-onset group. Many subjects in the late-onset group described predominantly oral symptoms with peanut ingestion. Our late-onset peanut allergy group might represent individuals with pollen-associated food allergy.⁴ In fact, cross-reactivity of peanut with birch and grass pollens has been reported.^{5,6} However, we did not find differences between pollen SPT response size between our early- and late-onset allergy groups. More specific epitope analysis might be required to detect these relationships.

One subject (Table II, subject 12) in the late-onset group deserves description. She had consumed peanut products

TABLE I. Patient characteristics

Characteristic	Early onset	Late onset	P value
No.	25	10	—
Age (y; median [range])	28 (15-61)	35 (16-53)	.20
Female sex (%)	13 (54)	4 (40)	.52
Age of diagnosis (y; median [range])	3 (0.5-10)	24.5 (10-53)	<.001
Asthma history*	16 (64)	5 (50)	.81
Allergic rhinitis history* (indoor allergens)	14 (56)	6 (60)	.78
Allergic rhinitis history* (seasonal allergens)	16 (64)	8 (80)	.78
Eczema history*	12 (48)	1 (10)	.35
Tree SPT (mm; median [range])	3.5 (0-15)	3.5 (0-6.5)	.98
Grass SPT (mm; median [range])	3.0 (0-13.5)	1.8 (0-10.5)	.95
Tree nut allergy reported (%)	16 (64)	7 (70)	.91
Any positive tree nut SPT response (%)	16 (64)	6 (60)	.83
Peanut SPT (mm; median [range])	5.3 (0-21.5)	2.9 (0-7.5)	.03
Peanut IgE (kU/L; median [range])	2.5 (<0.35 ->100)	0.4 (<0.35 -5.93)	.05
No. reporting a severe reaction ever (%)	23 (92)	5 (50)	<.01
Tolerance by means of DBPCFC (%)	4 (16)	3 (30)	.52

SPT, Skin prick test; DBPCFC, double-blind, placebo-controlled food challenge.

*Childhood or adult.

TABLE II. Characteristics of subjects undergoing food challenge

Onset	Outcome	Subject no.	Current age (y)	Peanut SPT (mm)	Peanut IgE (kU/L)	Years since last reaction*	Cumulative challenge dose (%)	Symptoms at food challenge
Early	Passed	1	21	1.5	2.5	5	—	—
		2	24	0	0.54	8	—	—
		3	45	3	<0.35	33	—	—
		4	19	2	3.97	11	—	—
	Failed	5	28	8.5	1.35	24	—	—
		6	28	10	<0.35	5	5	O
		7	27	3	<0.35	25	30	LR
		8	28	4	<0.35	8	100	O
Late	Passed	9	34	0	<0.35	13	—	—
		10	43	7.5	0.37	28	—	—
		11	29	5.5	0.43	1	—	—
	Failed	12	53	2.75	0.69	3	75	LR
		13	25	2	0.88	2	100	S, LR

SPT, Skin prick test; O, oral pruritus, swelling, or both; LR, lower respiratory (cough, wheezing, or both); S, skin pruritus, urticaria, or both.

*Or since age at peanut allergy diagnosis, if made on the basis of SPT response and no prior reaction.

regularly for many years. During an allergy evaluation at age 50 years, a positive skin test response to peanut was identified, and she was told to avoid peanut. Her pn-IgE level was 0.69 kU/L. Peanuts were strictly avoided for 3 years before she underwent a food challenge, during which she experienced lower respiratory tract symptoms. She was sensitized to peanut, as evidenced by positive skin and IgE test results, but was previously tolerant on the basis of clinical history. Once she began strict avoidance, tolerance was lost, and she experienced clinical reactivity. Loss of tolerance in a sensitized individual caused by avoidance has been reported in children who outgrew peanut allergy and then had a new allergy when they continued to avoid the food⁷ but has not been reported in adults. Practitioners should use caution when interpreting food allergy testing and always interpret results in light of the clinical history.

In summary, we identified 2 groups of individuals with peanut allergy: those who react with early exposure to peanuts and those who react years after ingesting peanut as a regular part of their diet. In both groups some subjects outgrew their allergy, supporting a role for oral food challenges past childhood. As in children, we identified adults with negative IgE levels who failed a food challenge, underscoring that a negative IgE result does not exclude clinical reactivity. Given our small sample size, it is not possible to determine whether late-onset peanut allergy is the same disease as early-onset peanut allergy or whether it is a distinct clinical syndrome, perhaps occurring primarily as a result of cross-reactivity with pollens.

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Ozone enhances markers of innate immunity and antigen presentation on airway monocytes in healthy individuals

To the Editor:

Elevated levels of ambient ozone (O₃) are associated with increased respiratory morbidity in the United States, and epidemiologic studies have reported