

Food reintroduction rates following negative oral food challenges to peanut and hazelnut: a survey study

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Clinical Implications

- Eighty-five percent of patients in our cohort successfully incorporated peanut and hazelnut into their diet after a negative food challenge. The rate of food avoidance increased as time from the challenge increased.

TO THE EDITOR:

An oral food challenge (OFC) that does not result in a clinical reaction is termed a *negative* or *passed* challenge. After a negative OFC, it is important that the patient incorporate the tested food in the diet regularly to maintain tolerance; therefore, instructions for food introduction should be provided and regular ingestion of the food encouraged.¹⁻³

Despite counseling to reintroduce the food, approximately 25% to 32% of patients do not eat the food after a negative challenge.⁴⁻⁶ In a retrospective cross-sectional study, in 28% of 269 negative OFCs the food was not reintroduced into the diet; peanut and hazelnut were significantly less likely than egg or milk to be reintroduced.⁴ Approximately 25% of those not introducing the food reported symptoms with reintroduction. In another survey, 25.4% of 71 negative OFCs did not reintroduce the food and peanut was less likely to be reintroduced compared with other foods.⁵ More recently, a study at our institution found that, among 85 patients who underwent a total of 109 negative OFCs, 20% were never or rarely (few times a year) ingesting the food.⁷ Peanut and tree nuts accounted for the majority (60%) of foods that were never or rarely ingested; however, the authors did not state if they corrected for the fact the majority of OFCs were to tree nuts.

We sought to identify factors that deter families from introducing nuts after a negative OFC and if birch pollen sensitization and oral allergy syndrome could affect the successful reintroduction of nuts. We emailed an anonymous survey (available in this article's Online Repository at www.jaci-inpractice.org) to patients who underwent peanut or hazelnut OFC at our institution. Surveys were sent directly to patients 18 years and older and to the caregivers of children younger than 18 years old. Responders were able to report on both peanut and hazelnut OFCs and for multiple children. The Icahn School of Medicine Institutional Review Board approved this study. Data were analyzed using the χ^2 and Fisher's exact tests. For questions with multiple responses, we applied Bonferroni correction resulting in an alpha of $0.05/n$, where n is the number of possible responses.

We emailed 981 surveys to patients with scheduled OFCs to peanut or hazelnut and collected data from 431 participants

(44% response rate) reporting 410 negative challenges (234 to peanut, 176 to hazelnut) between October 2011 and August 2017 (Figure E1, available in this article's Online Repository at www.jaci-inpractice.org). Sixty-five percent of the patients were male; 90% were Caucasian. The most common age at the time of survey completion was 1 to 5 years. Sixty percent of responders had a graduate degree and 67% reported an annual household income of more than \$150,000. Four hundred twenty-five caregivers responded on behalf of the patient; 24 caregivers responded for a second patient in the family. Six patients responded on their own behalf and 91% self-identified as the patient's mother. Eighty-five percent of patients reintroduced peanut after a negative peanut OFC; of those, 93% reported eating it at least once a month. Eighty-four percent were eating peanut butter; 48% were eating whole peanuts. Among 32 patients who continued to avoid eating peanut, the most common reason was patient refusal (50%); 3 patients did not know it was important to reintroduce peanut and 2 were worried about having a reaction. Eighty-four percent of patients reported receiving instructions to reintroduce peanut after the challenge. Fifteen patients reported symptoms at home; 8 were not treated and continued to ingest peanut. Those who avoided peanut after a reaction at home reported more symptoms compared with those who reintroduced peanut despite symptoms; the mean number of symptoms was 2.1 ± 1.1 versus 1.1 ± 0.4 , $P = .05$. Patients who continued peanut ingestion despite experiencing symptoms were older than those who discontinued it ($P = .04$). Three patients received epinephrine; 5 went to the emergency department (ED). One patient reported relapse of eosinophilic esophagitis and discontinued peanut.

Eighty-four percent of patients with a negative hazelnut OFC reintroduced hazelnut at home; of those, 90% reported eating it at least once a month. The majority of patients (95%) were eating hazelnut chocolate spreads; 10% were eating whole hazelnuts. Of the 26 patients who avoided hazelnut, the most common reason was refusal (52%); 5 patients feared having an allergic reaction despite a negative challenge and 2 patients did not know it was important to incorporate it. Seventy-three percent of patients reported receiving instructions to incorporate hazelnut after a negative OFC. Seven patients reported symptoms on reintroduction; 4 discontinued hazelnut, whereas 3 continued to ingest it. Patients who avoided hazelnut after a reaction reported more symptoms than those who continued to eat hazelnut despite having symptoms; the mean number of symptoms was 1.8 ± 0.5 versus 1.0 ± 0.0 , though this difference was not significant ($P = .06$). No patient received epinephrine or went to the ED.

There were no significant differences between those who did and did not introduce nuts regarding age, gender, race, ethnicity, and atopic history (Tables I and II). Patients with a history of anaphylaxis to peanut were less likely to introduce it after a negative OFC ($P = .04$); however, this result may be a biased because patients could have experienced anaphylaxis after passing the OFC. We did not find differences in reported springtime allergies between those eating nuts and those reporting

TABLE I. Patient characteristics and primary outcome analysis for negative peanut OFC

Patient characteristics	No peanut reintroduction after negative OFC (N = 32)		Reintroduced peanut after negative OFC (N = 179)		P value
	No. observed	n (%)	No. observed	n (%)	
Gender (male)	32	17 (53.1)	175	106 (60.6)	.43*
Ethnicity (non-Hispanic)	32	30 (93.8)	172	163 (94.8)	.68†
Age (y)	31		175		.43†
0-1		1 (3.2)		3 (1.71)	
1-5		9 (29.0)		69 (39.4)	
6-10		11 (35.5)		55 (31.4)	
11-17		10 (32.3)		40 (22.9)	
>18		0 (0.0)		8 (4.6)	
Years since completing OFC	32		179		.01‡
Less than a year ago		9 (28.1)		78 (43.6)	
1-2 y ago		5 (15.6)		49 (27.4)	
More than 2 y ago		18 (56.3)		52 (29.1)	
Avoiding the following food(s)§	27		115		
Tree nut		21 (77.8)		92 (80.0)	.80*
Other		13 (48.1)		52 (45.2)	.78*
History of anaphylaxis after ingestion of any food	32	13 (40.6)	174	81 (46.6)	.54*
Food(s) with history of anaphylaxis§	12		81		
Peanut		5 (41.7)		12 (14.8)	.04†¶
Hazelnut		2 (16.7)		5 (6.2)	.22†
Other		10 (83.3)		71 (87.7)	.65†
Instructed to eat peanut at home after the OFC	32	24 (75.0)	179	154 (86.0)	.11*
Noted symptoms while eating peanut at home after the OFC	31	5 (16.1)	179	10 (5.6)	.051†
Symptoms when eating peanuts after negative OFC	5		9		
Itchy mouth or throat		2 (40.0)		4 (44.4)	
Stomach pain, nausea, vomiting, or diarrhea		4 (80.0)		1 (11.1)	
Skin rash or itching		4 (80.0)		4 (44.4)	
Did not feel like yourself		1 (20.0)		1 (11.1)	
Other		1 (20.0)		1 (11.1)	

OFC, Oral food challenge.

* χ^2 test result.

†Fisher's exact test result.

‡Cochran-Armitage trend test.

§Multiple responses possible; each category was compared individually at $\alpha = 0.05$ with Bonferroni correction.

¶Result may be biased because patient could have experienced anaphylaxis after the OFC.

symptoms after a negative OFC. There was a negative association between time since completing peanut and hazelnut OFC and reintroduction of nuts; as time since completing peanut and hazelnut OFC increased, the rate of *not* eating the food also increased (Cochran-Armitage trend, $P = .01$ and $P = .001$, respectively).

Our study included a larger number of negative OFCs than previous studies and focused on peanut and hazelnut exclusively. To recruit a large number of patients we emailed anonymous surveys. The major limitation of this study is that all data were patient reported, subject to recall bias and not confirmed with the medical record. We have no data on peanut and hazelnut sensitization and the questionnaire is not validated. In addition, young patients refusing the food may be having mild symptoms they cannot describe. The population was 90% Caucasian, highly educated, and affluent; thus the results may not be generalizable.

The majority of patients (85%) reported reintroducing peanut and hazelnut after a negative OFC, more than previously reported. This may be partially explained by our practice of providing routine discharge instruction with the strong and consistent emphasis on reintroduction of the food into a regular diet, as well as a highly educated patient population. The most common reason for not introducing the food was patient refusal. Collectively, 9 patients (2%) discontinued the nut after noting symptoms with reintroduction. OFCs can have false negatives, possibly secondary to cofactors that may increase reactivity and decrease the threshold for a reaction including infections, exercise, nonsteroidal anti-inflammatory drug, or alcohol use.⁸ We did find that as time since completing peanut and hazelnut OFC increased, the rate of avoiding peanut and hazelnut also increased. Physicians should consider providing follow-up after a negative OFC to give guidance, discuss possible reactions, and ensure that patients are incorporating nuts into the diet.

TABLE II. Patient characteristics and primary outcome analysis for negative hazelnut OFC

Patient characteristics	No hazelnut reintroduction after negative OFC (N = 26)		Reintroduced hazelnut after negative OFC (N = 139)		P value
	No. observed	n (%)	No. observed	n (%)	
Gender (male)	26	20 (76.9)	138	90 (65.2)	.24*
Ethnicity (non-Hispanic)	26	24 (92.3)	138	126 (91.3)	>.99†
Age (y)	25		138		.18*
0-1		0 (0.0)		0 (0.0)	
1-5		6 (24.0)		37 (26.8)	
6-10		8 (32.0)		50 (36.2)	
11-17		6 (24.0)		42 (30.4)	
>18		5 (20.0)		9 (6.5)	
Years since OFC	26		139		.001‡
Less than a year ago		4 (15.4)		53 (38.1)	
1-2 y ago		7 (26.9)		51 (36.7)	
More than 2 y ago		15 (57.7)		35 (25.2)	
Currently avoiding following food(s)§	23		131		
Peanut		13 (56.5)		83 (63.4)	.53*
Tree nut		18 (78.3)		96 (73.3)	.62*
Other		6 (26.1)		37 (28.2)	.83*
History of anaphylaxis after ingestion of any food	26	13 (50.0)	136	77 (56.6)	.53*
Food(s) with history of anaphylaxis§	13		77		
Peanut		7 (53.8)		41 (53.2)	.97*
Hazelnut		1 (7.7)		3 (3.9)	.47†
Other		9 (69.2)		50 (64.9)	>.99†
Instructed to eat hazelnut at home after the OFC	26	17 (65.4)	138	102 (73.9)	.37*
Noted symptoms while eating hazelnut at home after the OFC	25	4 (16.0)	139	3 (2.2)	.01†
Symptoms when eating hazelnuts	4		3		
Itchy mouth or throat		2 (50.0)		1 (33.3)	
Stomach pain, nausea, vomiting, or diarrhea		2 (50.0)		0 (0.0)	
Skin rash or itching		3 (75.0)		1 (33.3)	
Did not feel like yourself		0 (0.0)		0 (0.0)	
Other		0 (0.0)		1 (33.3)	

OFC, Oral food challenge.

* χ^2 test result.

†Fisher's exact test result.

‡Cochran-Armitage trend test.

§Multiple responses possible; each category was compared individually at alpha = 0.05 with Bonferroni correction.

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No funding was received for this work.

Conflicts of interest: A. Nowak-Węgrzyn is employed by the Icahn School of Medicine, NY; receives grants from DBV Technologies, Astellas Pharma, Sanofi Aventis, Nutricia, Nestle; royalties from Up To Date; serves on the advisory boards for the Gerber Institute; is a member of the Data Monitoring Committee for Merck, Alk Abello, Sanofi Aventis; and is the deputy editor for the *Annals of Allergy Asthma and Immunology*. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication June 21, 2018; revised October 18, 2018; accepted for publication October 19, 2018.

Available online November 1, 2018.

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<https://doi.org/10.1016/j.jaip.2018.10.031>

REFERENCES

1. Fleischer DM, Conover-Walker MK, Christie L, Burks AW, Wood RA. Peanut allergy: recurrence and its management. *J Allergy Clin Immunol* 2004;114:1195-201.
2. Busse PJ, Nowak-Węgrzyn AH, Noone SA, Sampson HA, Sicherer SH. Recurrent peanut allergy. *N Engl J Med* 2002;347:1535-6.
3. Nowak-Węgrzyn A, Assa'ad AH, Bahna SL, Bock SA, Sicherer SH, Teuber SS, et al. Work Group report: oral food challenge testing. *J Allergy Clin Immunol* 2009;123(Suppl):S365-83.
4. van der Valk JP, Gerth van Wijk R, Vergouwe Y, de Jong NW. Failure of introduction of food allergens after negative oral food challenge tests in children. *Eur J Pediatr* 2015;174:1093-9.
5. Eigenmann PA, Caubet JC, Zamora SA. Continuing food-avoidance diets after negative food challenges. *Pediatr Allergy Immunol* 2006;17:601-5.
6. van Erp FC, Boot J, Knulst AC, Pasmans SG, van der Ent CK, Meijer Y. Reintroduction failure after negative peanut challenges in children. *Pediatr Allergy Immunol* 2014;25:580-5.
7. Gau J, Wang J. Rate of food introduction after a negative oral food challenge in the pediatric population. *J Allergy Clin Immunol Pract* 2017;5:475-6.
8. Versluis A, van Os-Medendorp H, Kruizinga AG, Blom WM, Houben GF, Knulst AC. Cofactors in allergic reactions to food: physical exercise and alcohol are the most important. *Immun Inflamm Dis* 2016;4:392-400.

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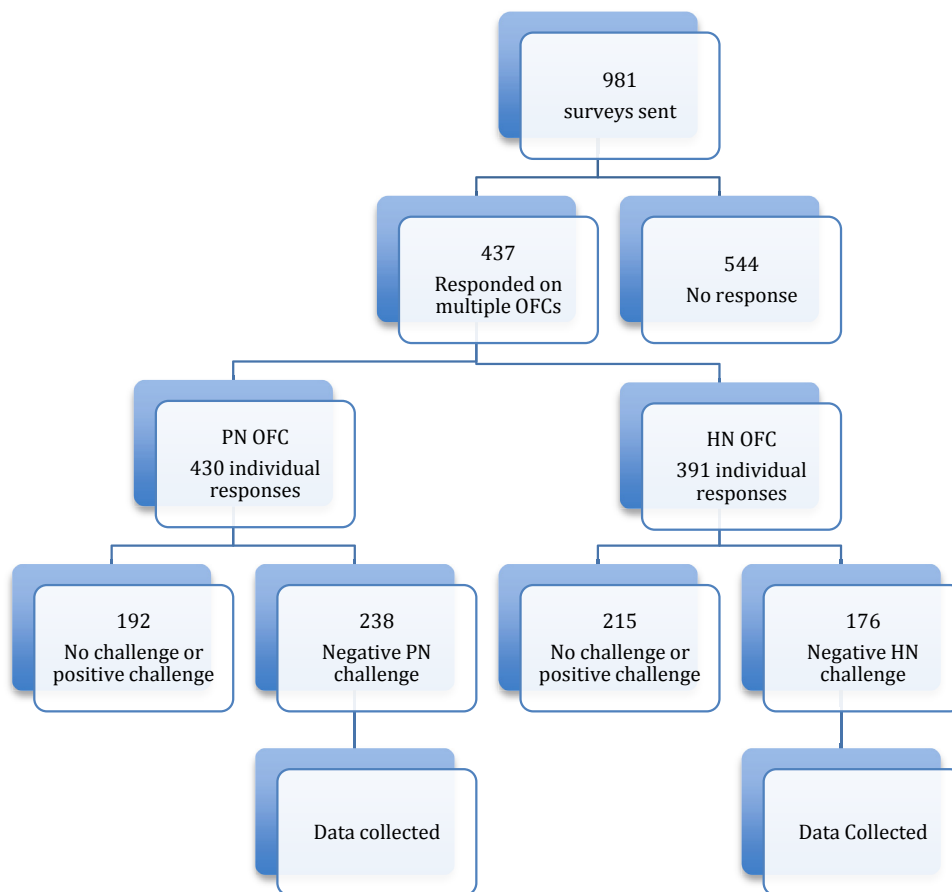


FIGURE E1. Enrollment flow diagram. *HN*, hazelnut; *OFC*, oral food challenge; *PN*, peanut.