Original Article

Successful Introduction of Peanut in Sensitized Infants With Reported Reactions at Home

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What is already known about this topic? Infants with allergic reactions to peanut at home and sensitization to peanut are often classified as peanut allergic.

What does this article add to our knowledge? Most infants with allergic reactions at home to peanut after early introduction have negative open oral food challenges, even when sensitized to peanut. After a negative challenge, peanut can be reintroduced to prevent further development of peanut allergy.

How does this study impact current management guidelines? A clinical peanut challenge is required to diagnose peanut allergy under the age of 12 months in infants with skin or gastrointestinal symptoms to peanut at home, even in the presence of sensitization.

BACKGROUND AND OBJECTIVE: Previous studies have shown efficacy of early introduction of peanut to prevent peanut allergy. It is currently unknown which diagnostic pathway is optimal after parental-reported reactions to peanut at home after early introduction.

METHODS: The PeanutNL cohort study included high-risk infants who were referred for early introduction of peanut. A subgroup of 186 infants with reactions to peanut at home underwent peanut skin prick tests and a supervised open oral food challenge (OFC) at a median age of 8 months. After a negative OFC, peanut was introduced at home.

RESULTS: Sensitization to peanut was detected in 69% of 186 infants, of whom 80% had >4 mm wheals in skin prick tests. An OFC with a cumulative dose of 4.4 g of peanut protein was performed in 163 infants with Sampson severity score grade I-III reactions at home; 120 challenges were negative. Peanut was subsequently introduced at home in infants with a negative challenge outcome. After 6 months, 96% were still eating peanut and 81% ate single portions of 3.0 g of peanut protein. One patient was considered to be peanut allergic after reintroduction of peanut at home.

CONCLUSIONS: These data show that 65% of infants with reported reactions to peanut at home have negative OFCs. In those children, peanut could be introduced safely, and 96% were able to consume peanut regularly without reactions. Challenging infants younger than 12 months prevents the misdiagnosis of peanut allergy and enables safe continued exposure to peanut and the induction of long-term tolerance. **(J Allergy Clin Immunol Pract 2024;■:■-■)**

Key words: *Peanut allergy; Prevention; Mislabeling; Open food challenge; Infants; Early introduction*

Since the publication of the Learning Early About Peanut Allergy (LEAP) trial in 2015,[1] timely introduction of peanut has been shown to reduce the development of peanut allergies in infants with atopic dermatitis. However, the LEAP trial did not study infants with reactions to peanut at home, or children who

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This study was financially supported by an unrestricted grant from the Reinier de Graaf Hospital Scientific Board (No. 6218.005).
Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication April 29, 2024; revised August 22, 2024; accepted for publication August 25, 2024.
Available online ■■
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2213-2198

https://doi.org/10.1016/j.jaip.2024.08.047

Abbreviations used
FPIES- Food protein—induced enterocolitis syndrome
LEAP- Learning Early About Peanut Allergy
OFC- Open oral food challenge
SCORAD- Scoring Atopic Dermatitis

were moderately to strongly sensitized to peanut. A total of 76 Infants in the LEAP trial with >4 mm sensitization to peanut without any observed reactions to peanut were excluded from the trial and advised to avoid peanut. At the age of 5 years, 78% of those children had a challenge-confirmed peanut allergy.[2] Currently, it is unclear whether children with skin prick tests >4 mm could benefit from food challenges in infancy and what the optimal diagnostic pathway is for infants with reactions at home after early introduction of peanut.

The Early Introduction Advice to Prevent Peanut and Egg Allergy was issued in 2017 by the Dutch Society of Pediatrics[3] and promotes early introduction of peanut at home and referral of high-risk infants to pediatric allergology centers for clinical introduction or for analysis after a reaction to peanut at home. The PeanutNL cohort consists of 892 high-risk infants who were included after referral by primary care physicians, pediatricians, or dermatologists between the ages of 4 and 12 months. The additional inclusion criteria were Scoring Atopic Dermatitis (SCORAD) eczema score >15 or previous immediate reaction to food or first degree relative with (pea)nut allergy. Of the 892 infants included in the cohort, 706 were referred for the clinical introduction of peanut and had never eaten peanut before. They have been described previously.[4] Reactions to peanut at home were reported in an additional 186 infants, and they were referred for analysis and advice considering ingestion of peanut. Infants who introduced peanut at home and did not have reactions were not referred and therefore not included in the cohort.

The contribution of open food challenges to the diagnosis of peanut allergy in infants with reactions to peanut at home was evaluated in those 186 infants, even in those with positive skin prick tests. The primary outcomes of the study were the percentage of infants with a negative open peanut challenge and subsequent continued ingestion of peanut at home, up to 6 months after the food challenge.

PATIENTS, AND MATERIALS AND METHODS

Patients

The 186 patients with prior reactions to peanut were included in the PeanutNL cohort at 1 of the 6 participating nonacademic pediatric allergology centers in the Netherlands: Reinier de Graaf Hospital, Delft (n = 123); Noordwest Ziekenhuisgroep, Alkmaar (n = 33); Deventer Ziekenhuis, Deventer (n = 13); Martini Ziekenhuis, Groningen (n = 10); Elkerliek Ziekenhuis, Helmond (n = 4); and Catharina Ziekenhuis, Eindhoven (n = 2). Patients were included between February 1, 2018, and January 1, 2021.

Severity of eczema was classified using the SCORAD classification.[5] Because atopic dermatitis disease activity varies over time, SCORAD was scored based on the average severity of atopic dermatitis in the months before inclusion as provided by the parents. Severity grading of allergic reactions at home was classified as described previously.[6]

The study protocol was judged by the Medical Ethical Committee Zuid-Holland West, which concluded that this study was not within the scope of the Medical Research Involving Human Subjects Act in the Netherlands. The study was conducted according to the Declaration of Helsinki. All parents or caregivers provided written informed consent for participation in the study. Patient data were collected in a Good Clinical Practice—certified database (Castor EDC, Amsterdam, the Netherlands).

MATERIALS AND METHODS

The skin prick test to peanut was chosen as the modality to detect sensitization to peanut because it directly allows comparison with the results of the LEAP study and because the results of skin prick tests are available on the day of testing. Skin prick tests were conducted with in-house produced peanut extracts in 169 (91%) patients included in Delft, Alkmaar, and Deventer as previously described,[7] or commercial whole peanut extract (ALK-Abelló, Hørsholm, Denmark) in the other 3 centers, and performed and analyzed as described previously.[8]

Open oral food challenges (OFCs) were performed in the 6 participating pediatric allergology centers under the supervision of a pediatric allergologist, pediatrician, or specialized nurse practitioner. Either commercially available peanut butter or defatted peanut powder (Golden Peanut Company, Alpharetta, Ga, or Sukrin, Lillestrom, Norway) was blended through mashed vegetables or fruit. The following dose-escalation schedules were used based on peanut skin prick tests: 0 to 4 mm wheal to peanut: 4-step challenge (100, 300, 1000, and 2000 mg of peanut protein) and >4 mm wheal to peanut: 8-step challenge (1, 3, 10, 30, 100, 300, 1000, and 3000 mg of peanut protein). All doses were given at 30-minute intervals with at least 60-minute observation after the final step. Special attention was paid to avoid local skin contact during the challenges. Allergic reactions were treated according to the Dutch guideline "Anaphylaxis in Children"[9] and classified as described previously.[6] As rescue medication, oral antihistamine (desloratadine or cetirizine), intramuscular or inhaled adrenaline, intravenous saline solution, ondansetron, and nebulized salbutamol were available.

After a negative challenge, parents were advised to introduce peanut at home and to administer at least 2000 mg of peanut protein cumulatively every week for at least 6 months, and to eat peanut regularly thereafter. Oral antihistamine was routinely available at home. After a positive challenge, parents were instructed to avoid peanut. Follow-up evaluation documenting adherence of peanut ingestion and tolerance to peanut was scheduled 4 weeks and 6 months after the challenge. In one center (Reinier de Graaf Hospital, Delft), an additional follow-up was available between the ages of 24 and 36 months.

Statistical analysis was performed using SPSS (version 25; IBM, Chicago, Ill). The association between a positive peanut challenge and the following items was analyzed: type of skin reaction, localization of skin reaction, timing of skin reaction after ingestion, Sampson severity grade, reports of vomiting, frequency of vomiting, timing of vomiting, and involvement of a specific tract. Pearson's χ^2 test was used for univariable analysis of categorical data (Fisher's exact test was used in small subpopulations).

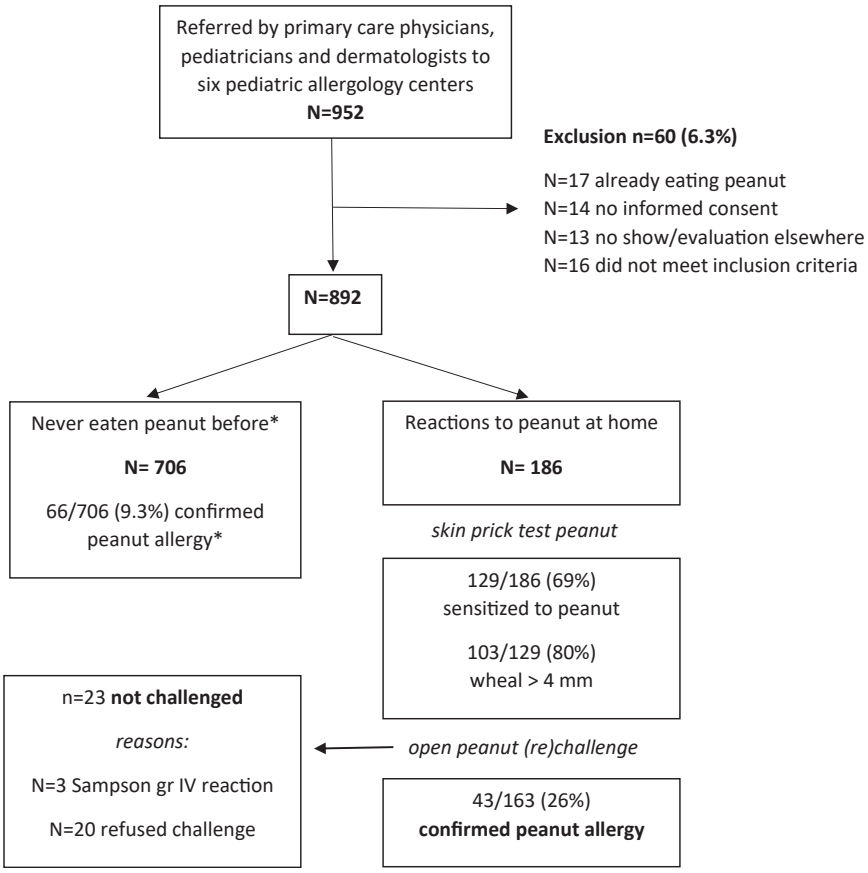

FIGURE 1. Screening and inclusion of the PeanutNL cohort. Infants (4-12 months) with a high risk of food allergy were referred according to the Early Introduction Advice to Prevent Peanut and Egg Allergy (2017) issued by the Dutch Society for Pediatrics.[3] *Children who never ate peanut before and were referred for first clinical introduction of peanut due to higher risk of reactions to peanut were not included in the analysis of this article and were described previously.[4]

RESULTS

The PeanutNL cohort: inclusion and patient characteristics

The PeanutNL cohort included 892 infants, of whom 706 (79%) had never eaten peanut before. That subgroup was described previously.[4] This article describes the results of a subgroup of 186 infants (21%) who had reactions to peanut at home at first introduction (Figure 1). These infants had a median age of 8 months, and 89% of them had atopic dermatitis with a median SCORAD of 28. A total of 88% of those infants had first degree family members with atopic disease, and 12% had a first degree relative with a (pea)nut allergy (Table I).

Severity of reactions to peanut at home

As shown in Figure 2, 98% of the infants referred were reported to have had Sampson severity score grade I-III reactions to peanut at home. In 3 of 186 infants (1.6%), the reaction at home was classified as a Sampson grade IV reaction with respiratory involvement.

A total of 163 of 186 infants (88%) presented with skin symptoms, of which 94 (58%) with erythema and 69 (42%) with urticaria and/or angioedema. In total 57 children (35%) had generalized skin reactions; in 106 children (65%), the skin reactions were localized (face/neck/hands). In 149 infants (91%), the skin reaction occurred within 2 hours after ingestion. Forty-seven of 186 infants (25%) presented with gastrointestinal symptoms, of whom 40 were vomiting and 7 appeared to have abdominal pain or oral allergy. Thirteen infants (7%) were reported to have upper airway symptoms after ingestion of peanut, of whom 12 had rhinitis or rhinoconjunctivitis.

Skin prick tests and peanut challenges in children with reactions to peanut at home

All 186 infants underwent skin prick tests with peanut extracts. In 69% of the infants (129 of 186), the skin prick test was positive. A total of 80% (103 of 129) of infants with positive skin prick tests to peanut had skin prick test wheals >4 mm (Figure 2). Skin prick tests were negative in 57 infants (31%) despite a history of previous reactions to peanut.

All parents were asked for permission to perform a supervised OFC with peanut, with exception of the 3 children presenting with Sampson grade IV respiratory symptoms. A total of 163 of 183 parents (89%) consented to a clinical peanut challenge (Figure 2). The 20 infants who were not challenged because of missing parental consent had larger peanut skin prick test wheals (median 9 mm vs median 5 mm) than those who were challenged.

TABLE I. Patient characteristics of the PeanutNL subcohort with reactions to peanut at home (N = 186)

Characteristic	Value	Additional remarks
Sex, male	57%	
Median age at inclusion	37 wk	IQR: 10 wk
Eczema	165 (89%)	
Median SCORAD	28	IQR: 23 SCORAD
Family history of primary (pea)nut allergy	22 (12%)	
Asthma/wheezing	16 (8.6%)	
History of immediate reactions to egg	31 (17%)	14/31 (45%) Sampson II-IV*
History of immediate reactions to cow's milk	14 (7.5%)	7/14 (50%) Sampson II-IV*
Exclusively or partially breastfed	162 (87%)	
First degree family member with atopic disease	164 (88%)	
Pets at home	52 (28%)	
Smoking at home	21 (11%)	
Consumption of peanut at home	177 (95%)	
Consumption of hazelnut at home	157 (84%)	
Consumption of cashew nut at home	156 (84%)	

IQR, Interquartile range; *SCORAD*, Scoring Atopic Dermatitis.
*Allergic reactions were graded according to Sampson.[6]

The outcome of 9 challenges (5.6%) was inconclusive, mainly due to refusal to eat the complete dose of the peanut containing matrix. All 9 infants had conclusive results after a second OFC: 5 did not have a peanut allergy and 4 had positive challenges. The results of the second challenge were used in the final analysis.

A total of 120 of 163 infants (74%) with Sampson severity score grade I-III reactions at home had negative OFCs, of whom 50 had negative skin prick tests and 70 had positive skin prick tests to peanut.

In 2 infants with negative skin prick tests, clinical challenges were not performed because parents did not consent to a challenge, and those patients belong to the 23 infants excluded from analysis; one of those presented with multiple reactions of late vomiting compatible with food protein–induced enterocolitis syndrome (FPIES). Five infants with negative skin prick tests had positive OFCs, and all 5 were diagnosed with FPIES based on the symptoms during challenge (Figure 2). They all had a history of vomiting to peanut at home. None of them required intravenous medication or saline solution. Of the 43 infants with positive challenges, 2 were administered intramuscular adrenaline (4.7%): 1 infant with repeated vomiting and 1 infant with a hoarse voice with inspiratory stridor.

A total of 7.7% (2 of 26) of infants with 1 to 4 mm skin prick tests to peanut had positive OFCs, as compared with 41% (31 of 76) of those with 5 to 9 mm and 83% (5 of 6) of those with ≥10 mm skin prick test wheals to peanut.

Predictability of parental-reported symptoms to challenge proven peanut allergies

To evaluate the contribution of parental-reported symptoms to the final diagnosis of peanut allergy as assessed by a clinical challenge, χ^2 analysis was performed on symptoms with the challenge result as an outcome. Of all the symptoms reported, only the type of skin reaction, the timing of the skin reaction after ingestion of peanut, and the severity of gastrointestinal symptoms were significantly associated with challenge-proven peanut allergies.

A total of 16% (14 of 90) of the children with reported erythema/eczema exacerbation without urticaria had a positive OFC, whereas 40% (21 of 53) of the infants with reported urticaria or angioedema had positive challenges ($P = .001$, χ^2). Erythema occurred within 60 minutes after peanut ingestion in 81% (73 of 90) of those infants. A total of 58 of 90 (64%) infants with erythema had positive skin prick tests, and 41 of 58 (71%) had wheals of ≥4 mm. In comparison, 45 of 53 (85%) infants who presented with urticaria had positive skin prick tests, and 36 of 45 (80%) had wheals ≥4 mm.

None of the 14 infants with late skin reactions (11 erythema and 3 urticaria) occurring >2 hours after ingestion had a positive challenge outcome, whereas 35 of 129 (27%) of infants with immediate skin reactions <2 hours after ingestions had positive OFCs ($P = .025$, χ^2). Infants with delayed skin reactions often had negative skin prick tests (9 of 14, 64%).

Fisher's exact analysis revealed significance in the comparison between a positive challenge and single time vomiting (18% peanut allergy, 3 of 17) and multiple times vomiting (57% peanut allergy, 8 of 14) after ingestion of peanut (including 5 patients with FPIES; $P = .031$).

The parental-reported pattern of skin reaction (ie, local vs systemic), the grade of skin reaction, vomiting as a symptom, the involvement of a specific tract, or the Sampson grade of reactions were not significantly discriminating between positive and negative peanut challenge outcomes.

Introduction of peanut at home after negative peanut challenges

After open peanut challenges were performed, 120 infants with a negative challenge were advised to reintroduce peanut at home. It was recommended to continue ingestion of at least 2.0 g of peanut protein per week in 1 or multiple doses, based on the EAT study.[10] For 118 children, follow-up on the reintroduction of peanut at home was available. In 2 children, the introduction of peanut at home did not succeed because of refusal to eat peanut at home. They did not have any evident allergic reactions, and both those children introduced peanut

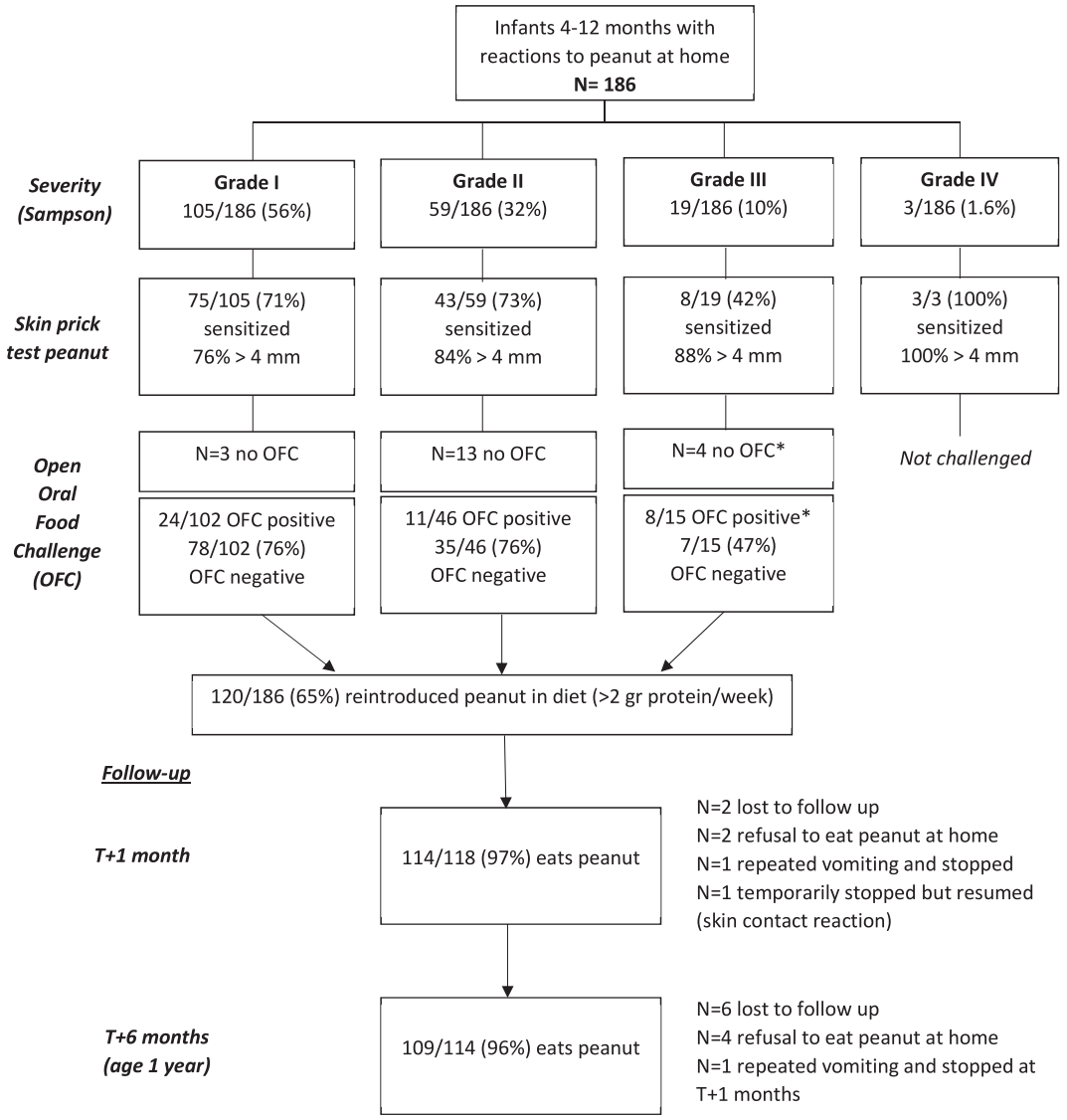

FIGURE 2. Evaluating peanut allergy and reintroduction of peanut in infants with reactions to peanut at first introduction. A total of 186 infants with prior reactions to peanut were assessed using Sampson's severity grading and skin prick tests. Of these, 120 infants had a negative OFC (3.4-4.4 g of peanut protein) and went on to introduce peanut at home, with follow-up assessments at +1 and +6 months. *One infant who presented with repeated vomiting without sensitization, with a phenotype compatible with FPIES, was not challenged. Five children with grade III reactions and without sensitization to peanut presented with a phenotype of FPIES at OFC. *FPIES*, Food protein–induced enterocolitis syndrome; *OFC*, open oral food challenge.

without reactions after the second year of life. In 116 infants, peanut was reintroduced at home within 4 weeks after the negative challenge.

A total of 108 of 116 parents (93%) did not report reactions to peanut at home, 4 weeks after the challenge. Eight parents reported reactions within the first 4 weeks of reintroduction of peanut at home: 5 reports of local skin contact reactions, 2 reports of a single episode of vomiting, and 1 infant reacted with vomiting multiple times. In the infant with repeated vomiting, peanut introduction at home was stopped, and the infant was considered peanut allergic. In 1 patient with local skin contact reactions to peanut, ingestion of peanut was temporarily halted, but resumed a few weeks later—without reactions. In the other 6 infants with local skin contact reactions or mild (single episode) vomiting, peanut ingestion was continued. Two infants with reported skin reactions after reintroduction of peanut had negative skin prick tests before the challenge; the other 6 infants with reported reactions after reintroduction had positive skin prick tests (range: 4-7 mm).

At 4 weeks after the challenge, 114 infants were actively eating peanut (Figure 2). Of 114 infants, 105 (92%) managed to eat at least the advised dose of 2.0 g of peanut protein per week (10 g of peanut butter). Reported adherence to continued reintroduction of peanut at home was 93% because 106 of 114 parents reported to have given peanut to their infants at least 3 out of the 4 weeks after the challenge.

Follow-up of peanut ingestion and reactions to peanut after introduction of peanut at home

At 6 months after the peanut challenge, follow-up data were available for 114 infants (Figure 2).

A total of 96% of the infants were eating peanut, of whom 81% (88 of 109) were eating single portions of at least 3.0 g of peanut protein. Five infants were not eating peanut: 1 classified as peanut allergic at 4 weeks after the challenge due to multiple episodes of vomiting. The other 4 were not eating peanut because of refusal (including 2 infants who refused to eat peanut at 4 weeks after the negative challenge). All 4 children refusing to eat peanut at 4 weeks or 6 months after the challenge introduced peanut in their diet without reactions in the second year of life.

In 4 infants, new reactions to peanut were reported, all of which were skin contact reactions. These children continued to eat peanut, and over time, these skin reactions were not reported anymore.

All parents were advised to continue to eat peanut *ad libitum* after 6 months of regular peanut exposure. Tolerance to peanut between the ages of 2 and 3 years was evaluated in the largest participating center (Reinier de Graaf Hospital, Delft). Of the 82 children from that center with negative peanut OFCs, follow-up data were available for 78 children at the age of 24 to 36 months. In none of the children, new reactions to peanut were reported. Of 78 children, 77 (99%) were still eating peanut in the 3 months before evaluation. In 1 case, parents did not give peanut without a specific reason. Of the 77 children, 86% (66) were able to eat single portions of at least 3.0 g of peanut protein without reactions. A total of 74 of 77 (96%) infants were eating peanut at least once a month without reactions, and 59 of those children had weekly ingestion of peanut.

DISCUSSION

The results from the PeanutNL cohort demonstrate the contribution of performing skin prick tests and open peanut challenges when parents report reactions to peanut at home at first introduction in infancy. In 65% (120 of 186) of the infants with reactions to peanut at home, a supervised open food challenge was negative, and reintroduction of peanut at home proved to be safe and efficient, with 96% reporting long-term tolerance.

The PeanutNL cohort study is one of the first studies to demonstrate that vigorously deploying open food challenges in infants allows prevention of peanut allergy, even in those with immediate reactions to peanut and even if they are sensitized to peanut. At least 65% of infants who were referred for advice after reactions to peanut at home could introduce peanut and continued to ingest peanut without major reactions. Due to the exclusion of 23 infants from OFCs and because OFCs are at risk of interpretation bias, that number might even be an underestimation. To minimize the risk of interpretation bias during the OFC, it is of note that the centers were instructed to discriminate between local contact reactions in the face (considered nonallergic if the final dose of the challenge was ingested without further symptoms) and systemic skin reactions.

The observation that 31% of the infants with reported reactions to peanut at home did not have sensitization to peanut demonstrates that mislabeling of reactions by parents is common and the contribution of the presenting symptoms to discrimination between allergy and tolerance is limited.

Half of the parents (n = 90) reported erythema as an immediate reaction to peanut in this study. This proved to be a poor predictor of a positive challenge, with only 14 infants (16%) having a challenge-proven peanut allergy. Erythema in children with atopic dermatitis is common and might be the result of several mechanisms, among which irritative or immunological mechanisms. Erythema or skin contact reaction was the most common temporary side effect seen on reintroduction of peanut at home, but continued exposure in those cases was associated with long-term tolerance to peanut. It could be hypothesized that erythema might also be a sign of immune activation due to tolerance induction, rather than the development of an allergy. Therefore, excluding food proteins from the diet after a reaction of erythema or increased atopic dermatitis should be avoided unless there is a positive food challenge for the culprit food. In addition, recent randomized studies show that treatment of atopic dermatitis with topical steroids reduces food allergies by 25% to 40%.[11,12] This is the preferential way to deal with eczema flare-ups or erythematous reactions after IgE-mediated allergies have been excluded.

Next to mislabeling of allergic reactions, an alternative explanation of the observed tolerance to peanut could be that infants with sensitization to peanut were in a prestage of peanut allergy and successful introduction of peanut after a negative challenge is facilitated by secondary prevention. Data from the LEAP study have shown that 78% of the infants who were excluded from the trial because of skin prick tests >4 mm had challenge-proven peanut allergies at the age of 5 years.[2] In the current study, 46 of 82 infants (56%) with skin prick tests >4 mm and reactions at home were tolerant and reintroduced peanut at home. This shows that a cutoff value of 4 mm to diagnose a peanut allergy will lead to overdiagnosis of peanut allergy in infants aged <12 months and that in over half of those children, a peanut allergy could be prevented. In this regard, it should be noted that 91% of the infants in the PeanutNL subcohort were tested using in-house produced peanut extracts. The LEAP study used a commercial lyophilized peanut extract that was used in 9% of the infants in the current analysis.[1] Because peanut extract—induced wheals might vary between home-made and commercial preparations,[7] this may hamper a direct comparison with the LEAP data.

In the development of peanut allergy, there might be a prestage with peripheral allergic reactions, due to local crosslinking of IgE on mast cells in the skin. This may result in local allergic skin reactions, similar to the ones observed in the PeanutNL cohort. In those infants, systemic tolerance seems to be easily achievable by gastrointestinal exposure to the allergen at this young age, as is suggested by the follow-up data in this study. In this respect, it is interesting to see that there are reports of increased efficacy and even long-term tolerance when peanut immunotherapy is conducted at a young age, especially <3 years.[13-17] Reactions to peanut at home in the PeanutNL cohort might be mislabeling of peanut allergy in those with negative skin prick tests, but there will also be cases where reintroduction is a means to execute secondary prevention. In those cases, the concepts of oral food immunotherapy may apply. Various mechanisms may play a role in the efficacy of oral food immunotherapy in preschool children, one of which could be a lack of IgE directed against linear epitopes to peanut before the age of 30 months, as has been recently shown in samples from the LEAP cohort.[18] This could be an explanation why reintroduction of

peanut was so successful in this cohort of children <12 months of age.

In summary, the results from this cohort study demonstrate the contribution of supervised open peanut challenges in achieving long-term tolerance to peanut in children with reactions to peanut at home in infancy. Rather than avoiding challenges because of the age of those infants, there is a role for pediatrician-allergologists in conducting peanut challenges in this young population. This will result in less overdiagnosis of peanut allergies and increased opportunities to develop tolerance due to continued oral ingestion of peanut.

Acknowledgments

The authors wish to acknowledge the following people who were part of the regional study teams and actively participated in collection and registration of data: Reinier de Graaf Hospital: Pascalle Andela, Marloes Elgersma, Lotty Koerse, Fabienne Bal, Ismahaan Abdisalaam, Kelly van der Vorst, Timo Verheggen; Martini Hospital: Irene Herpertz, Gerbrich van der Meulen, Arvid Kamps, Geertje Hofstra, Alisa Boxem, Maria Huijssoon; Noordwest Alkmaar: Jeroen Hol, Yvonne Duijvestijn, Annette Blauw; Deventer Hospital: Monique Gorissen, Joyce Faber, Daphne Philips, Annelies van der Kolk; Elkerliek Hospital: Suzanne Fleuren; Catharina Hospital: Loes Kooijman, Hanneke Wijnberg, Wendy Verheijen, Trudy van Mierlo.

REFERENCES

1. Du Toit G, Roberts G, Sayre PH, Bahnson HT, Radulovic S, Santos AF, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. N Engl J Med 2015;372:803-13.
2. Du Toit G, Tsakok T, Lack S, Lack G. Prevention of food allergy. J Allergy Clin Immunol 2016;137:998-1010.
3. Klok T, Verhoeven DHJ. Preventing food allergy: avoid avoidance. Ned Tijdschr Allergie Astma 2017;17:157-65.
4. Verhoeven DHJ, Herpertz ICEM, Hol J, Klok T, Fleuren SPM, Hendriks T, et al. Reactions to peanut at first introduction in infancy are associated with age ≥8 months and severity of eczema. Pediatr Allergy Immunol 2023;34:ei13983.
5. European Task Force on Atopic Dermatitis. Severity scoring of atopic dermatitis: the SCORAD index: consensus report of the European Task Force on Atopic Dermatitis. Dermatology 1993;186:23-31.
6. Sampson HA. Anaphylaxis and emergency treatment. Pediatrics 2003;111:1601-8.
7. Terlouw S, van Boven FE, Borsboom-van Zonneveld M, de Graaf-In 't Veld C, van Splunter ME, van Daele PLA, et al. Homemade food allergen extracts for use in skin prick tests in the diagnosis of IgE-mediated food allergy: a good alternative in the absence of commercially available extracts? Nutrients 2022;14:475-87.
8. Heinzerling L, Mari A, Bergmann KC, Bresciani M, Burbach G, Darsow U, et al. The skin prick test—European standards. Clin Transl Allergy 2013;3:3-13.
9. Dutch Guideline Database. Anaphylaxis in children. 2021. Accessed October 19, 2023. https://richtlijnendatabase.nl/richtlijn/anafylaxie_bij_kinderen/startpagina_-_anafylaxie_bij_kinderen.html
10. Perkin MR, Logan K, Tseng A, Raji B, Ayis S, Peacock J, et al. Randomized trial of introduction of allergenic foods in breast-fed infants. N Engl J Med 2016;374:1733-43.
11. Miyaji Y, Yang L, Yamamoto-Hanada K, Narita M, Saito H, Ohya Y. Earlier aggressive treatment to shorten the duration of eczema in infants resulted in fewer food allergies at 2 years of age. J Allergy Clin Immunol Pract 2020;8:1721-4.
12. Yamamoto-Hanada K, Kobayashi T, Mikami M, Williams HC, Saito H, Saito-Abe M, et al. Enhanced early skin treatment for atopic dermatitis in infants reduces food allergy. J Allergy Clin Immunol 2023;152:126-35.
13. Jones SM, Kim EH, Nadeau KC, Nowak-Wegrzyn A, Wood RA, Sampson HA, et al. Immune Tolerance Network. Efficacy and safety of oral immunotherapy in children aged 1-3 years with peanut allergy (the Immune Tolerance Network IMPACT trial): a randomised placebo-controlled study. Lancet 2022;399:359-71.
14. Vickery BP, Berglund JP, Burk CM, Fine JP, Kim EH, Kim JI, et al. Early oral immunotherapy in peanut-allergic preschool children is safe and highly effective. J Allergy Clin Immunol 2017;139:173-81.
15. Herlihy L, Kim EH, Burks AW, Barber H, Cook Q, Yang L, et al. Five-year follow-up of early intervention peanut oral immunotherapy. J Allergy Clin Immunol Pract 2021;9:514-7.
16. Barten LJC, Zuurveld M, Faber J, Garssen J, Klok T. Oral immunotherapy as a curative treatment for food-allergic preschool children: current evidence and potential underlying mechanisms. Pediatr Allergy Immunol 2023;34:e14043.
17. Loke P, Vickery BP, Jones SM, Peters RL, Roberts G, Koplin JJ. Food allergen immunotherapy in preschool children: do we have the evidence? J Allergy Clin Immunol Pract 2023;11:1028-35.
18. Suarez-Farinas M, Suprun M, Bahnson HT, Raghunathan R, Getts R, duToit G, et al. Evolution of epitope-specific IgE and IgG4 antibodies in children enrolled in the LEAP trial. J Allergy Clin Immunol 2021;148:835-42.