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The prevalence of peanut-triggered food protein-induced enterocolitis syndrome in a prospective cohort of infants introducing peanut in the first year of life

Dirk H. J. Verhoeven[1,2] | Geertje Hofstra[3] | Joyce Faber[4] | Olga Benjamin-van Aalst[5] | Mijke Breukels[6] | Tom Hendriks[7] | Roy Gerth van Wijk[2] | Hans de Groot[1]

[1]Department of Pediatrics, Reinier de Graaf Hospital, Delft, The Netherlands

[2]Section of Allergology and Clinical Immunology, Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands

[3]Department of Pediatrics, Martini Hospital, Groningen, The Netherlands

[4]Pediatrics Allergy Treatment Centre, Deventer Hospital, Deventer, The Netherlands

[5]Department of Pediatrics, Northwest Clinics, Alkmaar, The Netherlands

[6]Department of Pediatrics, Elkerliek Hospital, Helmond, The Netherlands

[7]Department of Pediatrics, Catharina Hospital, Eindhoven, The Netherlands

Correspondence
Dirk H. J. Verhoeven, Department of Pediatrics, Reinier de Graaf Hospital, P.O. Box 5011, 2600 GA Delft, The Netherlands.
Email: dirk.verhoeven@rdgg.nl

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Abstract

Background: Since the early introduction of peanut to prevent IgE-mediated peanut allergy, other case series have suggested an increased incidence of peanut-triggered Food Protein Induced Enterocolitis Syndrome (FPIES). Data on the prevalence of peanut-induced FPIES in prospective cohorts are lacking.

Methods: The PeanutNL cohort is a prospective cohort that included infants at risk of peanut allergy ($n = 706$) as well as infants with reactions to peanut at home after early introduction ($n = 186$). They all introduced peanut before the age of 12 months. Oral food challenges were performed to introduce peanut or to evaluate reactions to peanut at home.

Results: Of the 706 infants that were included for first introduction of peanut, 2 had reactions with a phenotype compatible with FPIES (0.3%). Of the 186 infants with reactions to peanut at home, 6 were diagnosed with FPIES (3.2%). Seven out of 8 cases had ingestions of peanut without reactions at home or during clinical introduction before FPIES became apparent. During a 3-year follow-up, six infants (75%) were shown to be tolerant to peanut before the age of 3 years.

Conclusion: The prevalence of challenge-proven peanut-induced FPIES in a Dutch cohort of atopic infants that introduced peanut between the ages of 4 and 11 months is 0.3%. The majority of cases were tolerant to peanut before the age of 3 years. When introducing peanut in the first year of life, physicians should be aware of FPIES reactions, but it should not be a reason to avoid early introduction of peanut.

KEYWORDS
early introduction, FPIES, infants, peanut allergy, prevention

Abbreviations: FPIES, Food Protein Induced Enterocolitis Syndrome; OFC, Oral Food Challenge; SCORAD, Scoring Atopic Dermatitis.

1 | INTRODUCTION

The benefits of early introduction of peanut in the first year of life to the prevention of peanut allergy have been demonstrated by the Learning Early About Peanut Allergy (LEAP) study.[1] Since the early introduction of peanut, several publications have addressed an apparent increase in the amount of infants presenting with Food Protein Induced Enterocolitis Syndrome (FPIES) caused by the ingestion of peanut.[2–7] The hallmarks of this disease are severe vomiting within 1–4 h of ingestion of the culprit food and at least 3 minor criteria, as was published in an international consensus guideline 2017.[8] The incidence of FPIES to any food is reported to be 0.51%–0.7% in children (in the USA and Spain, respectively)[9,10] and for cow's milk 0.34% (in Israel).[11] The reports detailing an increased prevalence of peanut-induced FPIES are derived from case series with an increased presentation of patients with reaction to peanut. There is a lack of data regarding the prevalence of peanut-induced FPIES following early peanut introduction in a large, unselected cohort of infants at risk for peanut allergy.

The PeanutNL cohort has been described previously[12,13] and is a cohort of 892 infants from atopic parents. These infants had eczema or immediate reactions to food and they were screened for peanut allergy in the Netherlands before the age of 12 months. A large part of this cohort (706 infants) had never ingested peanut before, which means that there is no prior selection bias to select for FPIES reactions. Another subpopulation of 186 infants was referred due to reactions to peanut at home and is therefore a biased subpopulation. The infants in the PeanutNL cohort were analyzed using skin prick tests (SPT) to peanut and an oral food challenge (OFC). Regular ingestion of peanut at home after a negative OFC was evaluated at 4 weeks and 6 months after the study visit. The primary end goal was a negative peanut challenge. One of the secondary goals was to register the prevalence of peanut-induced FPIES in this cohort. Furthermore, resolution of peanut-induced FPIES was evaluated between the ages of 2–3 years with a follow-up OFC peanut in peanut FPIES patients from both subcohorts.

Key message

The prevalence of peanut-induced FPIES after early introduction of peanut in atopic infants is 0.3%. 75% of these children were shown to be tolerant to peanut between the ages of 2 and 3 years.

2 | PATIENTS, MATERIALS AND METHODS

2.1 | Patients

After screening, 892 patients were included in the PeanutNL cohort. They were screened between the 1st of February 2018 and the 1st of January 2021 at one of the six participating pediatric allergology centers: Reinier de Graaf, Delft $n = 520$; Martini Ziekenhuis, Groningen $n = 131$; Northwest clinics, Alkmaar $n = 123$; Deventer Ziekenhuis, Deventer $n = 76$; Elkerliek Ziekenhuis, Helmond $n = 25$; Catharina Ziekenhuis, Eindhoven $n = 17$. They were referred by primary care physicians, pediatricians, and dermatologists according to the "Early Introduction Advice to Prevent Peanut and Egg Allergy" issued by the Dutch Society for Pediatrics.[14]

The primary inclusion criteria for the study were an age between 4 and 12 months and either mild/moderate-to-severe eczema (SCORAD ≥15) and/or previous immediate reactions to food other than peanut and/or a first-degree family member with systemic reactions to (pea) nut. A total of 706 infants with no prior exposure to peanut fulfilled the primary inclusion criteria. Furthermore, 186 infants aged 4–12 months with immediate reactions to peanut at first introduction at home were also included in the cohort, as a separate subpopulation.

Severity of eczema was classified using the SCORAD classification.[15] Since atopic dermatitis disease activity varies over time, SCORAD was scored based on the severity of atopic dermatitis in the months prior to inclusion as provided by the parents.

The study protocol was reviewed by the Medical Ethical Committee Zuid-Holland West (METC registry number 17–106), 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 study database (CASTOR EDC, Amsterdam, the Netherlands).

2.2 | Materials and methods

Skin prick tests were performed with in-house produced or commercial peanut extracts as previously described.[12,13] Serologic determination of peanut-specific IgE in the third year of life was determined according to the manufacturer's instructions (ImmunoCap, Thermo Fisher Scientific, Uppsala, Sweden, and ImmuLite, Siemens Healthineers, Erlangen, Germany).

Open oral food challenges (OFC) were performed in the food challenge units of the 6 participating pediatric allergology centers under supervision of a pediatric allergologist, pediatrician, or specialized nurse practitioner as described previously.[12,13] Either commercially available peanut butter or defatted peanut powder (Golden Peanut Company, Alpharetta, GA, USA, or Sukrin, Lillestrom, Norway) was blended through mashed fruit or vegetables.

In case of a negative skin prick test to peanut and no prior exposure to peanut, a 2-step clinical introduction (200 and 2000 mg peanut protein) was performed and children were observed for at least 1 h. In case of previous reactions to peanut at home with suspicion of FPIES due to delayed vomiting and a negative skin prick

test, a 4-step challenge was performed with 30-min intervals (cumulative dose ≥3.4 g peanut protein with 2–4 h observation).

In case of previously diagnosed FPIES that fulfilled the diagnostic criteria,[8] a 3-step challenge was performed between the age of 2 and 3 years with 3 × 0.1 g/kg peanut protein and 4 h observation according to the Dutch FPIES Guideline issued by the Dutch Society of Pediatrics.[16]

Reactions which were compatible with an FPIES phenotype were treated according to the Dutch Guideline FPIES with ondansetron either orally, intramuscular, or intravenously and sodium chloride 0.9% intravenous fluid suppletion if necessary.

After a negative challenge, parents were advised to feed their infants at least 10 g of peanut butter (a cumulative dose of at least 2 g of peanut protein) per week for 6 months and consume peanut regularly thereafter. At 4 weeks and 6 months after the challenge, introduction of peanut at home and the occurrence of new reactions were evaluated. Infants that were diagnosed with peanut-induced FPIES were re-evaluated between the ages of 2 and 3 years.

3 | RESULTS

3.1 | Characteristics of the PeanutNL subcohort of infants that never ate peanut before

As shown in Figure 1 and Table 1, 706 infants that never ate peanut before were included for clinical introduction of peanut. They either had eczema with a SCORAD of ≥15 or a previous immediate reaction to food (mainly egg and milk) and/or a first-degree relative with a primary (pea)nut allergy. The characteristics of this subcohort have been described elsewhere.[12] In short, they had a median age of 26 weeks at inclusion (IQR 21.5–30.5 weeks), a median SCORAD eczema score of 30 (IQR 15–45), and 94% had at least one first-degree relative with atopic disease (eczema, food allergy, allergic rhinoconjunctivitis, or asthma). They introduced peanut at a median age of 6 months (IQR 4.5–7.5 months). Immediate reactions to food other than peanut was seen in 19% of the patients, with 67 parents reporting immediate reactions to milk and 58 parents reporting immediate reactions to egg. Since this subcohort of 706 infants was not exposed to peanut before, it is designated the "primary peanut introduction subgroup".

3.2 | Incidence of peanut-induced FPIES in the primary peanut introduction subcohort

All 706 infants underwent skin prick testing and clinical introduction of peanut, even if the skin prick test to peanut was negative. In 66 infants (9.3%), the challenge outcome of the OFC peanut was positive. In 64 infants, the reaction was immediate. In 2 infants (Table 1, DELF#1 and GRON#1), there was a delayed reaction with severe vomiting and 3 and 4 minor criteria for FPIES, respectively (Table 2, DELF#1 and GRON#1). They both had a negative skin prick tests to peanut. It is of note that the DELF#1 infant had a first, inconclusive OFC due to discomfort (crying) and itching without clear skin reactions. When trying to introduce peanut at home, there was a reaction with vomiting and

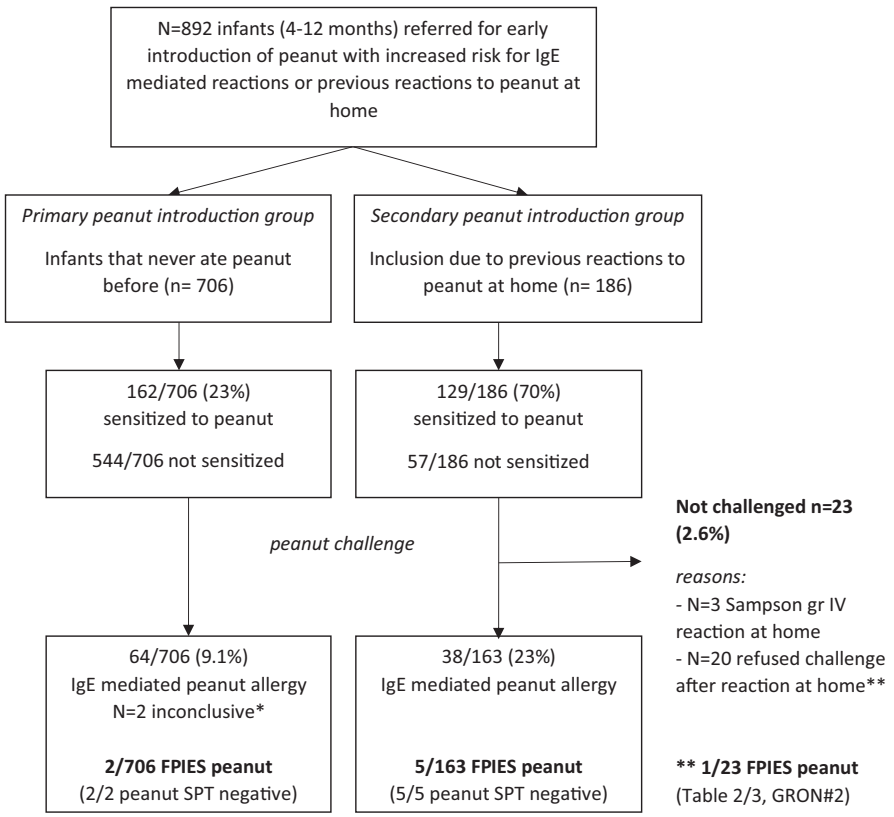

FIGURE 1 Overview of peanut FPIES in the PeanutNL cohort. A total of 8 peanut-induced FPIES cases were identified. All 8 infants had negative skin prick tests to peanut. The prevalence of peanut-induced FPIES in the subgroup that did not have reactions to peanut before the study visit was 2 out of 706 (0.3%). *Two infants had inconclusive challenge results after a second challenge due to refusal to eat the peanut containing matrix.

during a second OFC, symptoms compatible with a classical phenotype of peanut FPIES were observed. The GRON#1 patient reacted during the first exposure to peanut at the OFC, but had previous reactions to milk and avocado with a phenotype compatible with FPIES before. The details of the reactions are displayed in Table 2. Both patients were instructed to avoid peanut. The 640 patients with a negative

TABLE 1 Baseline characteristics of the primary and secondary peanut introduction groups in the PeanutNL cohort.

	Primary peanut introduction group ($n = 706$)	Secondary peanut introduction group (included due to reaction to peanut at home) ($n = 186$)
	n (%)	*n* (%)
Gender	425 (60%) male	105 (57%) male
Median age at inclusion	26 weeks (IQR: 9w)	37 weeks (IQR: 10w)
Median age at peanut challenge	6 months (IQR: 3 m)	8 months (IQR: 2 m)
Eczema	619 (88%)	165 (89%)
Median SCORAD	30 SCORAD (IQR: 30)	28 SCORAD (IQR: 23)
First degree relative with (pea)nut allergy	346 (49%)	22 (12%)
History of wheezing	63 (8.9%)	16 (8.6%)
History of immediate reactions to food	132 (19%)	186 (100%) to peanut
Egg	58 (8.2%)	31 (17%)
Cow's milk	67 (9.5%)	14 (7.5%)
Exclusively or partially breastfed	535 (76%)	162 (87%)
First degree family member with atopic disease	662 (94%)	164 (88%)
Consumption of peanut at home by other family members	536 (76%)	177 (95%)

Note: A total of 706 infants were included in the PeanutNL cohort that had never eaten peanut before and 186 infants were included due to reactions of peanut at home.

TABLE 2 Characteristics of peanut FPIES patients in the PeanutNL cohort.

Patient ID	Sex	Age at diagnosis	Eczema (SCORAD)	Previous reaction to peanut at home	Ingestions without reaction	SPT peanut	OFC peanut
DELF#1	F	34w	62	No	1[a]	0 mm	Yes, positive
GRON#1	M	21w	51	No	0	0 mm	Yes, positive
DEVE#1	F	28w	51	Yes: two times vomiting within 30 min without diarrhea, lethargy or discoloration	1	0 mm	Yes, positive
DELF#2	F	26w	40	Yes: Third and fourth ingestion repeated vomiting within 2–6 h without diarrhea, lethargy or discoloration.	2	0 mm	Yes, positive
DELF#3	M	26w	27	Yes: Third ingestion of peanut resulted in repeated vomiting without diarrhea, lethargy or discoloration.	2	0 mm	Yes, positive
DELF#4	F	42w	0	Yes: The fourth, fifth and sixth ingestion resulted in repeated vomiting after 2 h without diarrhea, lethargy or discoloration.	3	0 mm	Yes, positive
DELF#5	M	48w	22	Yes: Third ingestion repeated vomiting after 2 h without diarrhea, lethargy or discoloration.	2	0 mm	Yes, positive
GRON#2	F	34w	26	Yes: Vomiting 2 h after ingestion for multiple hours with lethargy and discoloration on 3 occasions.	2	0 mm	Not performed

Note: Patients DELF#1 and GRON#1 were diagnosed in the primary cohort that had never eaten peanut before. Patients DEVE#1, DELF#2–5 and GRON#2 were identified in the secondary cohort after a history of delayed vomiting after introduction of peanut at home.

Abbreviations: DELF, Reinier de Graaf, Delft; DEVE, Deventer Hospital, Deventer; F, female; GRON, Martini Hospital, Groningen; M, male; OFC, oral food challenge; SCORAD, scoring atopic dermatitis; SPT, skin prick test; w, weeks.

[a]Patient DELF#1 had an inconclusive first challenge without vomiting. Introduction of peanut at home resulted in vomiting after 1 h (see Table 3).

challenge were advised to introduce peanut at home. During follow-up at 4 weeks and 6 months, no further peanut-triggered FPIES reactions were reported. Quantified adherence to introduction of peanut was recorded in 605/640 infants (95%) with negative peanut challenges. At 4 weeks after the study visit, 90% ingested at least 2.0 g of peanut protein per week (10 g of peanut butter).

Concluding, the prevalence of peanut-induced FPIES in the primary peanut introduction group is 2 out of 706 infants (0.3%).

3.3 | Peanut-induced FPIES in the secondary peanut introduction subgroup

Next to the 706 infants that never ate peanut before, the PeanutNL cohort included 186 infants with reported reactions at home (Figure 1 and Table 1). Since this subcohort is biased for having increased incidence of reactions to peanut, including FPIES reactions, it was designated the "secondary peanut introduction subgroup". The characteristics of this subgroup have been described elsewhere.[13] In short, they had a median age of 8 months at food challenge (IQR 7–9 months), and 89% were diagnosed with atopic dermatitis with a median SCORAD of 28. First-degree relatives with any atopic disease were present in 88% of the cases. Skin prick test to peanut revealed that 129 of 186 infants (70%) with reactions to peanut at home were sensitized. A total of 19 infants presented with Sampson severity grade III anaphylactic type reactions after introducing peanut at home. In 10 of those 19 infants, there were no skin or respiratory symptoms, and in 9 out of 10, there was a reaction of vomiting multiple times with an onset >1 h after ingesting peanut. In 2 out of those 9 infants, skin prick tests were positive, and both were confirmed to have IgE-mediated peanut allergy after OFC. In the other 7 of those 9 infants, the skin prick test peanut was negative. One infant (GRON#2, Tables 1 and 2) had three reactions with severe delayed vomiting to peanut at home. There were 3 minor criteria for FPIES. Due to multiple reactions at home, the parents did not consent in an OFC peanut to confirm the peanut allergy. Since the infant fulfilled all the criteria for the diagnosis FPIES, she was diagnosed as such. The other 6 patients with negative skin prick tests and delayed vomiting at home were challenged with peanut, and OFCs were positive in 5 of them. All 5 had reactions with delayed vomiting during the OFC (characteristics displayed in Tables 1 and 2). One patient (DELF#4) had reproducible reactions to peanut with delayed vomiting on 4 different occasions, but failed to meet 3 minor criteria for FPIES. The infant was classified as mild FPIES.

Concluding, 6 infants in the secondary introduction subgroup were classified as having a peanut-induced FPIES (3.2%).

3.4 | Characteristics of infants with peanut-induced FPIES

As displayed in Tables 2 and 3, the mean age of the 8 peanut-induced FPIES patients was 32 weeks (standard deviation: 9.0 weeks) at diagnosis, and all of them had negative skin prick tests. All patients with reactions to peanut at home had 1–3 occasions of ingestion of peanut without reactions before FPIES reactions became apparent (Table 2). It is of note that the DELF#1 patient from the primary introduction cohort had an inconclusive first OFC (first introduction of peanut) and did not display an FPIES phenotype until multiple ingestions of peanut had occurred.

The average time between ingestion of peanut and vomiting was 1 h and 40 min (range: 1.0–2.5 h). Of the 7 patients that underwent an OFC, 6 infants (86%) had a last ingested dose of >2.0 g of peanut protein, equaling at least 11 peanuts (Table 2). Most infants reacted with marked discoloration ($n=6$, 75%) and lethargy ($n=4$, 50%), and 3 out of 8 (38%) presented with diarrhea within 24 h after the reaction.

3.5 | Resolution of peanut-induced FPIES between the ages of 2 and 3 years

All 8 infants diagnosed with peanut-induced FPIES avoided peanut in their diet. All parents were offered a challenge with peanut between the ages of 2–3 years (Table 4). Newly developed sensitization to peanut, although mild, was detected in 2 patients at that age. The parents of 7 out of 8 infants consented to a challenge with peanut. In 6 infants (75% of the patients diagnosed with peanut-induced FPIES in infancy), this challenge was negative, and peanut was successfully introduced in the diet in all of them during follow-up. All patients with newly developed sensitization to peanut had negative challenge outcome. The patient with mild FPIES (2 minor criteria at diagnosis) was the only patient that still reacted to peanut at the age of 2 years and 8 months, again with only 2 minor criteria.

4 | DISCUSSION

The results from the PeanutNL cohort are the first to demonstrate that the prevalence of challenge-confirmed peanut FPIES is 0.3% in infants that introduced peanut between the ages of 4 and 11 months. A case series of 8 patients with peanut FPIES was prospectively studied. The majority of infants (88%) had multiple ingestions of peanut without reactions before the FPIES phenotype became apparent (Table 2). Reaction thresholds to peanut were high, >2.0 g of peanut protein in 86% of the infants that underwent an OFC. Spontaneous resolution of peanut-induced FPIES and successful introduction of peanut in the diet was demonstrated in 6 out of 8 infants (75%) between the ages of 2–3 years.

The strengths of the PeanutNL cohort are that the data were prospectively collected in a relatively large cohort of atopic infants. Reactions were confirmed with open food challenges at diagnosis in 7 out of 8 peanut FPIES cases. The downside of the current study is that the cohort was selected for a higher risk for IgE-mediated peanut allergies. Since it has been reported that pediatric FPIES patients have an increased atopic comorbidity,[17] the reported prevalence

TABLE 3 Characteristics of peanut-induced FPIES reactions.

Patient ID	Severe vomiting	Timing vomiting after ingestion	Peanut protein consumed at OFC	Repeated reaction peanut	Similar reaction to other food	Lethargy	Discoloration	Diarrhea	First Aid visit	IV fluid	Hypotension	Hypothermia	Neutrophil count	No. minor criteria
DELF#1[a]	Y	1.5 h	3.4 g	Y, 2x[a]	–	Y	Y	N	Y	N	N	N	n/a	4
GRON#1	Y	1 h	2.2 g	N	Milk Avocado	N	Y	N	Y	Y	n/a	n/a	n/a	4
DEVE#1	Y	2.5 h	3.4 g	Y, 2x	Rice	N	N	Y	N	N	N	N	N	3
DELF#2	Y	2.5 h	0.2 g	Y, 3x	Rice	Y	N	Y	N	N	N	N	n/a	4
DELF#3	Y	1.5 h	2.2 g	Y, 4x	–	Y	Y	Y	Y	N	N	N	n/a	5
DELF#4	Y	1 h	3.4 g	Y, 4x	–	N	Y	N	N	N	N	N	n/a	2
DELF#5	Y	1.5 h	3.4 g	Y, 2x	Egg	N	Y	N	N	N	N	Y 35°C	n/a	4
GRON#2[b]	Y	2 h	n/a	Y, 3x	–	Y	Y	N	N	N	N	N	n/a	3

Note: Severe vomiting was defined as multiple occasions of forceful vomiting.

Abbreviations: g, grams; h, hours; N, no; n/a, not available; Y, yes.

[a]First challenge was inconclusive. Since the patient was not sensitized, home introduction was attempted by the parents, resulting in a reaction to peanut at home with vomiting after 1 h. A second clinical challenge was performed and severe vomiting after 1.5 h with discoloration and lethargy were observed.

[b]GRON#2 was not clinically challenged with peanut but 3 reactions were observed at home during which the symptoms were observed.

TABLE 4 Resolution of peanut FPIES.

Patient ID	Age first OFC	SPT peanut	Result first OFC	Age second OFC	SPT/sIgE peanut	Result repeat OFC	Reactions
DELF#1	8 months	0 mm	positive	n/a	n/a	n/a	No consent for OFC at 2 year 2 months and 3 year 8 months
GRON#1	5 months	0 mm	positive	2 year 7 months	1.4 kU/L	negative	
DEVE#1	6 months	0 mm	positive	1 year 9 months	n/a	negative	
DELF#2	6 months	0 mm	positive	2 year 1 months	<0.35 kU/L	negative	
DELF#3	6 months	0 mm	positive	3 year 0 months	<0.35 kU/L	negative	
DELF#4	9 months	0 mm	positive	2 year 8 months	0 mm	positive	Repeated vomiting, discoloration
DELF#5	11 months	0 mm	positive	2 year 6 months	3 mm[a]	negative	
GRON#2	n/a[b]	0 mm	n/a[b]	2 year 1 months	0 mm	negative	

Abbreviations: n/a, not available; OFC, oral food challenge; SPT, skin prick test.

[a]Saline control: 0 mm, histamine control 5 mm.

[b]Patient was not challenged at diagnosis due to lacking parental consent after 3 reactions to peanut at home.

from the PeanutNL cohort might be higher than that in the general population. The risk of missing FPIES patients due to spontaneous tolerance between a reaction at home and food challenges cannot be fully excluded. However, since the median age at OFC after a reaction at home was 8 months (with an interquartile range of 2 months), such development of tolerance would have to occur within months.

An increase in the incidence of peanut-induced FPIES has been suggested in single-center case series, with a main argument that the amount of peanut-induced FPIES patients has increased after early introduction of peanut was recommended to prevent IgE-mediated peanut allergy.[3] The current study reveals a prevalence of peanut-induced FPIES of 0.3% in infants at high risk of IgE-mediated peanut allergy, with population based estimates of pediatric FPIES to any food trigger varying between 0.5% and 0.7%.[9,10] The current study, nor the previous case reports can substantiate a direct causal relationship between peanut FPIES and early introduction of peanut. It remains unclear whether early introduction of peanut has increased the amount of peanut-induced FPIES cases, or merely increased the awareness of reactions to peanut and FPIES specifically after the publication of the diagnostic guideline in 2017.[8]

A total of 88% of the cases in the PeanutNL cohort study had ingestion of peanut without reactions before FPIES became apparent. All previously published case-series describing peanut-induced FPIES have reported a similar presentation: in 40%–67% of children that presented with peanut-induced FPIES, the initial introduction of peanut was without any reactions.[2–7] This is in contrast with IgE-mediated allergies, where reactions are often seen upon first exposure. The pathophysiology of FPIES is still poorly understood and may be multifactorial, involving innate immunity, adaptive immunity, autonomic dysfunction and the gut microbiome.[18] The activation of these components may explain why reactions are not always seen upon first exposure. Furthermore, reaction thresholds in cow's milk-induced FPIES have been reported to be high,[11] which also might explain why a first, low dose of peanut might not give any reactions. In the current study, 6 out of 7 infants reacted to more than 2000 mg peanut protein (11 peanuts) during the diagnostic OFC in infancy (Table 3).

A total of 6 out of 8 patients (75%) with peanut-induced FPIES were tolerant to peanut between the ages of 2–3 years, as shown by a clinical challenge and confirmed introduction of peanut at home after a negative challenge. In one patient, parents did not consent to a new challenge. Two infants developed sensitization to peanut under avoidance of peanut, but both passed the OFC without immediate reactions. The reported resolution rates of peanut-induced FPIES are scarce. The study of Rotella et al.,[7] which includes the patients reported by Lopes,[3] had follow up results for 14 out of 45 patients at a median age of 53 months, and 43% (6 out of 14) were challenge-proven tolerant to peanut. The study of Jungles et al.[6] had follow up results for 7 out of 14 patients at mean age of 24 months, and 71% (5 out of 7) passed a peanut challenge. Interestingly, the first study reports that children who did not outgrow peanut FPIES are older at time of the OFC: 7 out of 8 infants aged >3 years still had reactions to peanut, whereas 1 out of 6 patients aged <3 years had positive OFC results. The latter study reported the exact opposite: the two children that still had FPIES reactions to peanut were 15–17 months of age and 5 infants were tolerant at >20 months of age. These conflicting data might be due to a selection bias in case-series. The current study suggests that evaluation of peanut FPIES with a peanut challenge between the ages of 2 and 3 years could be considered for infants that present with peanut-induced FPIES after early introduction of peanut.

Concluding, the data from the PeanutNL cohort show that 0.3% of the infants that introduce peanut because they were at risk for IgE-mediated peanut allergy presented with FPIES symptoms. Clinicians should be aware that FPIES reactions can develop in the first weeks of peanut introduction, and not necessarily upon first introduction. It remains unclear whether peanut-induced FPIES is increased because of increased awareness for FPIES or due to early introduction of peanut in young infants. Nevertheless, the prognosis of peanut-induced FPIES in small case-studies (43%–75% resolution rates) is likely to be better than IgE mediated peanut allergies (29% resolution at the age of 6 years).[19] Therefore, the benefits of early introduction of peanut to prevent IgE mediated allergies outweigh the risk of peanut-induced FPIES. When introducing peanut in the first year of life, physicians should be aware of FPIES reactions, but it should not be a reason to avoid early introduction of peanut.

AUTHOR CONTRIBUTIONS

Dirk H. J. Verhoeven: Conceptualization; investigation; funding acquisition; writing – original draft; methodology; validation; visualization; writing – review and editing; formal analysis; project administration; data curation. **Geertje Hofstra:** Investigation; writing – review and editing; validation; data curation. **Joyce Faber:** Investigation; validation; writing – review and editing; data curation; project administration. **Olga Benjamin-van Aalst:** Investigation; data curation; writing – review and editing. **Mijke Breukels:** Investigation; writing – review and editing; project administration; data curation. **Tom Hendriks:** Investigation; project administration; data curation; writing – review and editing. **Roy Gerth van Wijk:** Conceptualization; writing – review and editing; supervision; methodology. **Hans de Groot:** Conceptualization; investigation; funding acquisition; methodology; writing – review and editing; supervision.

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The authors have no conflicting interests to disclose.

PEER REVIEW

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ORCID

Dirk H. J. Verhoeven https://orcid.org/0009-0004-3599-6888

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