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Peanut consumption habits and incidence of new peanut allergy in a cohort of younger siblings of peanut-allergic children

Maxime Paquin, MD, Louis Paradis, MD, François Graham, MD, Philippe Begin, MD, Anne Des Roches, MD



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1 **Peanut consumption habits and incidence of new peanut allergy in a cohort of**
2 **younger siblings of peanut-allergic children**

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5 Maxime Paquin, MD¹, Louis Paradis, MD¹⁻², François Graham, MD¹⁻², Philippe Begin,
6 MD¹⁻²⁻³ and Anne Des Roches, MD¹⁻³

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9 ¹Pediatric Allergy and Clinical Immunology, CHU Sainte-Justine, Montreal, Canada

10 ²Allergy and Clinical Immunology, Centre Hospitalier de l'Université de Montreal
11 (CHUM), Montreal, Canada

12 ³Applied Clinical Research Unit, CHU Sainte-Justine, Montreal, Canada

13

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15

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17 **Corresponding author:**

18 Anne Des Roches

19 3175 chemin de la Côte-Sainte-Catherine,

20 Montreal, Qc, Canada, H3T 1C5

21 Phone: (514) 345-4837

22 a.des.roches@umontreal.ca

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52 *Clinical Implications*

53 Minimal frequency of ingestion required to maintain tolerance is unknown in siblings of

54 patients with peanut allergy. In this follow-up of our FRATRIES cohort, we show that a

55 minimal monthly consumption was associated with a low risk of peanut sensitization.

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58 This decade has seen major changes in food allergy primary prevention. The LEAP and
59 LEAP-on trials showed that early peanut introduction (4 to 11 months) is associated with
60 a decreased risk of developing peanut allergy in high-risk children. Early peanut
61 introduction is now recommended in recent guidelines for high-risk children including
62 younger siblings of peanut-allergic children.¹⁻²⁻³

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64 Siblings of children with food allergy have an increased risk of developing peanut
65 allergy.⁴ The FRATRIES study was a diagnostic accuracy study specifically aimed at
66 peanut-naïve children with an older sibling diagnosed with peanut allergy.⁵ The median
67 ages of participants and their older allergic siblings were 23 months and 5 years,
68 respectively. Eczema was present in 38% of participants and 69% of their allergic sibling.
69 Other food allergy was present in 9,1% of allergic siblings (including 3,9% of egg
70 allergy). After double-blind skin testing the 154 participants underwent parent-led peanut
71 introduction in clinic, and 146 (95%) were found to be tolerant and were encouraged to
72 introduce peanut at home at least once a week.

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74 The minimal amount and frequency of peanut ingestion following introduction in high-
75 risk children is still debated. The LEAP study showed that 2 g of peanut protein three
76 times a week was effective at preventing allergy in both sensitized and nonsensitized high
77 risk children.¹ The EAT study patients who were from the general population ate at least
78 2 g of allergenic food protein of each of the six study foods per week. Intention-to-treat

analysis was not statistically significant but the per-protocol analysis of this study showed a 100% reduction in peanut allergy (0% versus 2.5%).⁶

As seen in the EAT study, adherence to a dietary intervention can be difficult to observe for families. Having an older child with peanut allergy may represent an additional obstacle to the regular introduction of allergenic foods in younger siblings. Parents usually prefer that non-allergic children eat the allergen outside the family home, which is bound to reduce the frequency of intake. After reviewing the literature, we found little data to support a lower consumption than what is suggested in LEAP or EAT in order to maintain tolerance in that population. There is a lack of published evidence that giving a lower dose and frequency of peanut than EAT is actually effective.

The purpose of the present follow-up study was to assess home peanut consumption and incidence of new peanut allergy in those children in the years following supervised introduction in clinic.

One-hundred-thirty-three (133) of the 146 peanut tolerant siblings (89.9%), were reached by phone at a median of 2.9 years (range: 1.8-4.2) following their participation in the FRATRIES study (Figure E1 in the Online Repository). Patients that reported eating peanut less than once a year, who had not introduced peanut, or who stopped eating peanuts due to suspected reaction, were invited for further assessment in clinic, including peanut skin prick tests, serum peanut-specific IgE and peanut oral food challenge (OFC).

Of the total reached, 2 (1.5%) ate peanut daily, 15 (11.3%) ate it weekly, 58 (43.6%) ate it monthly, 34 (25.5%) ate it several times a year, 6 (4.5%) ate it less than annually. Fifteen (11.3%) avoided peanuts completely. Finally, there were three patients (2.3%) who had been eating regularly (weekly, monthly and every three months) but stopped following a clinical reaction at home. A majority of families (97%) were able to estimate the child's consumption at a dose greater than 500 mg of peanut protein per dose, in peanut butter, peanut or candy containing peanuts.

Of the 24 siblings that did not eat peanut during the last year, 17 patients were assessed in the pediatric allergy clinic (Table I), while 7 declined the invitation. OFC was performed in 15 patients and only one patient who had been dosing every three months prior to a suspected reaction at home was confirmed allergic. The remaining two patients, who had been avoiding peanuts, declined confirmatory OFC because of high skin prick tests or specific IgE results, which were above the 95% predictive positive value for IgE-mediated allergy. None of the 3 newly diagnosed patients had eczema nor food allergy.

Based on these numbers, the observed risk of developing allergy was 0% (95%CI: 0 – 6) in patients eating at least once a month (n=77), 3% (95%CI: 0.5 – 15) in patients eating it less than monthly (n=41) and 18% (95%CI: 5 – 48) for patients on complete avoidance (n=15) (Figure 1).

Despite the advice to continue weekly consumption at home, only a small portion of patients in the original cohort (15.6%) ate peanuts at least once a week. Fifteen patients

(11.3%) had never introduced peanuts. Families unanimously gave as reason the fear of older sibling contamination. No sibling was on peanut oral immunotherapy (OIT).

This study shows that a monthly consumption seems to be protective in siblings of allergic children. None of the patients consuming peanuts at least monthly developed a new peanut allergy.

However, it should be noted that our studied population is older (median of 23 months) than the studies cited above. Allergic sensitization begins early and this is why tolerance induction studies start with very young patients (under 11 months usually). Eczema was also less prevalent in our study with 38% of siblings affected in comparison to the 90% of severe eczema in the LEAP consumption group. Our population, although less at risk, presents unique challenges. Since the allergy is already present at home, families are less inclined to rapid introduction and constant ingestion thereby limiting adherence to the aforementioned recommendations. Ideally, the treatment plan should include all family members, a minimal monthly consumption for non-allergic children and desensitization considered in allergic children in order to reduce family anxiety towards the allergen.

Although we studied older children (median 23 months), parents of siblings of allergic children should be advised to introduce the potential allergen at least monthly. Monthly consumption could be the compromise between the fear of contaminating the allergic child and the risk of developing new allergies in other siblings. Also, performing peanut OIT in older siblings may be an interesting avenue to help make regular exposure easier

148 in the younger sibling, which would be an additional family benefit of OIT in older
149 siblings. Finally, it is important to underline that siblings without severe eczema or egg
150 allergy are also a population at risk for peanut allergy and those families should receive
151 strong education efforts too. Further prospective studies with younger and a larger
152 number of patients are required to confirm these findings.

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194 Figures legend:

195 Figure 1. Observed risk of developing allergy to peanut based on consumption habits. P-
196 values were determined by Fisher exact test.

197 Table legend:

198 Table I. Individual subject data

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Table I. Individual subject data

ID	Sex	Age	Peanut consumption after initial evalutation	Initial Peanut allergy tests		Peanut allergy test at follow-up		Home reaction	Challenge
				SPT in mm (extract/fresh)	IgE (kU/l)	SPT in mm (extract/fresh)	IgE (kU/l)		
Diagnosed with peanut allergy									
19	F	5.9	Not introduced	- / 3	0.55	22 / 21	5.94	-	Declined
42	F	6.4	Every 3 months until reaction	- / -	0.15	11 / 12	0.93	Throat pruritus after consumption	+
112	M	3.7	Not introduced	- / -	< 0.10	n.a. / 8	24.2	Hive after direct skin contact	Declined
Peanut tolerant									
72	F	5.3	Once a week until reaction	- / 4	0.55	3/8	2.53	Urticaria of neck and throat, pruritus after consumption	-
91	M	3.9	Once a month until reaction	- / 3	< 0.10	- / -	n.a.	Throat pruritus after consumption	-
17	F	6.4	Less than once a year	- / -	< 0.10	- / -	n.a.	-	-
37	F	5.1	Less than once a year	- / -	< 0.10	- / -	n.a.	-	-
45	F	4.6	Not introduced	- / -	< 0.10	- / -	n.a.	-	-
54	F	6.7	Not introduced	- / -	< 0.10	- / -	n.a.	-	-
61	F	5.7	Not introduced	- / -	< 0.10	- / -	n.a.	-	-
66	M	6.8	Not introduced	- / -	< 0.10	- / -	n.a.	-	-
118	F	4.0	Not introduced	- / -	0.11	- / -	n.a.	-	-
126	F	3.4	Not introduced	- / -	< 0.10	- / -	n.a.	-	-
138	F	5.5	Not introduced	- / -	< 0.10	- / -	n.a.	-	-
140	M	8.1	Not introduced	- / -	< 0.10	- / -	n.a.	-	-
164	M	3.5	Not introduced	- / -	< 0.10	- / -	n.a.	-	-
198	F	3.5	Less than once a year	- / 2	< 0.10	- / -	n.a.	-	-
Declined appointment									
59	M	4.4	Less than once a year	- / -	< 0.10	n.a.	n.a.	-	n.a.
76	F	7.5	Not introduced	- / -	< 0.10	n.a.	n.a.	-	n.a.
88	F	7.4	Not introduced	- / -	< 0.10	n.a.	n.a.	-	n.a.
133	M	6.1	Less than once a year	- / -	< 0.10	n.a.	n.a.	-	n.a.
134	M	6.1	Less than once a year	+ / -	< 0.10	n.a.	n.a.	-	n.a.
154	M	3.6	Not introduced	- / -	< 0.10	n.a.	n.a.	-	n.a.
163	F	6.6	Not introduced	- / -	< 0.10	n.a.	n.a.	-	n.a.

+, positive; -, negative; n.a., not available

Figure 1. Observed risk of developing allergy to peanut based on consumption habits. P-values were determined by Fisher exact test.

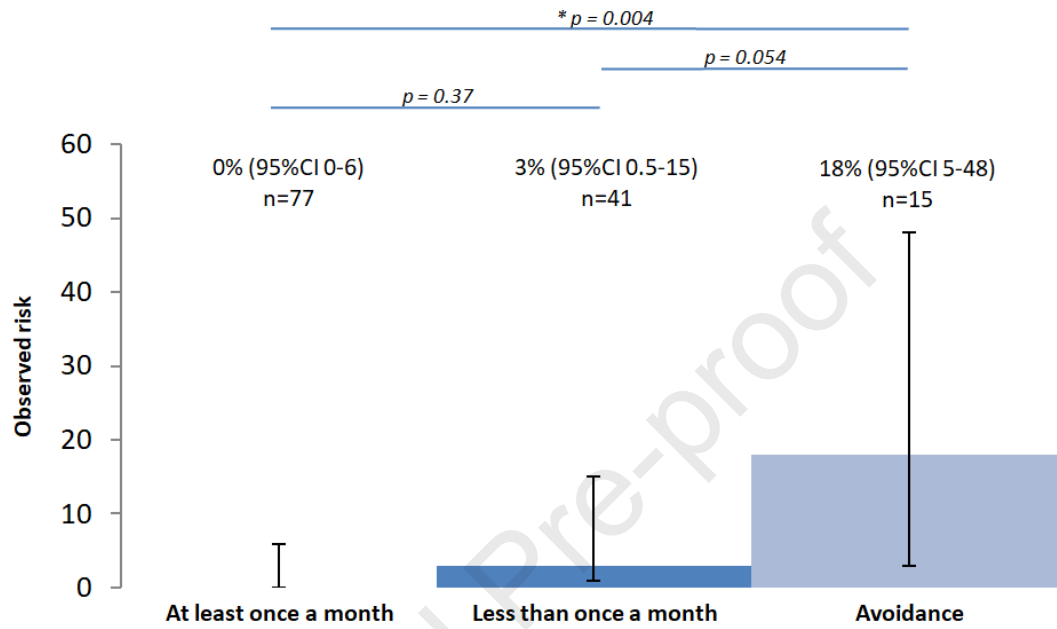


Figure E1. Enrollment flow diagram