

A randomized controlled study of peanut oral immunotherapy: Clinical desensitization and modulation of the allergic response

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Background: Open-label oral immunotherapy (OIT) protocols have been used to treat small numbers of patients with peanut allergy. Peanut OIT has not been evaluated in double-blind, placebo-controlled trials.

Objective: To investigate the safety and effectiveness of OIT for peanut allergy in a double-blind, placebo-controlled study.

Methods: In this multicenter study, children ages 1 to 16 years with peanut allergy received OIT with peanut flour or placebo. Initial escalation, build-up, and maintenance phases were followed by an oral food challenge (OFC) at approximately 1 year. Titrated skin prick tests (SPTs) and laboratory studies were performed at regular intervals.

Results: Twenty-eight subjects were enrolled in the study. Three peanut OIT subjects withdrew early in the study because of allergic side effects. During the double-blind, placebo-controlled food challenge, all remaining peanut OIT subjects ($n = 16$) ingested the maximum cumulative dose of 5000 mg

(approximately 20 peanuts), whereas placebo subjects ($n = 9$) ingested a median cumulative dose of 280 mg (range, 0–1900 mg; $P < .001$). In contrast with the placebo group, the peanut OIT group showed reductions in SPT size ($P < .001$), IL-5 ($P = .01$), and IL-13 ($P = .02$) and increases in peanut-specific IgG₄ ($P < .001$). Peanut OIT subjects had initial increases in peanut-specific IgE ($P < .01$) but did not show significant change from baseline by the time of OFC. The ratio of forkhead box protein 3 (FoxP3)^{hi}: FoxP3^{intermediate} CD4⁺ CD25⁺ T cells increased at the time of OFC ($P = .04$) in peanut OIT subjects.

Conclusion: These results conclusively demonstrate that peanut OIT induces desensitization and concurrent immune modulation. The current study continues and is evaluating the hypothesis that peanut OIT causes long-term immune tolerance. (*J Allergy Clin Immunol* 2011;127:654–60.)

Key words: Peanut allergy, oral immunotherapy, desensitization, food allergy

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Food allergy is a major health concern in industrialized countries, affecting approximately 3.9% of children.¹ Peanut allergy is one of the most common forms of food allergy, with approximately 3 million Americans reporting allergy to peanuts or tree nuts, and the prevalence appears to be increasing.² Peanut and tree nut allergy account for the vast majority of life-threatening or fatal allergic reactions to foods.^{3,4} In addition, peanut allergy is often lifelong.⁵ Current treatment options are limited to strict peanut avoidance and ready access to epinephrine. Challenges for patients and families with food allergy are considerable,⁶ and accidental ingestion is common.⁷ Anxiety impairs social functioning in individuals with food allergy, who report poorer health-related quality of life than those with diabetes mellitus.⁸

These findings underscore the need for active treatment strategies. Animal and human studies have examined potential therapies for peanut allergy, including allergen-nonspecific and allergen-specific modalities; however, recent meta-analyses highlight the shortage of controlled studies in the field.^{9,10} TNX-901, a humanized mAb, prevents binding of IgE to its high-affinity receptor on mast cells and basophils and was found to increase the threshold of peanut protein inducing symptoms in individuals with peanut allergy from less than 1 peanut to almost 12 peanuts.¹¹ However, the prohibitive cost of mAb treatment may limit this approach. A combination of traditional Chinese herbal medications, food allergy herbal formula 2, has shown promise in eliminating anaphylaxis to peanut in murine¹² and phase I studies.¹³

Allergen immunotherapy, an allergen-specific treatment, refers to the administration of increasing amounts of an allergen to individuals with IgE-mediated allergy to diminish the allergic

Abbreviations used

FoxP3: Forkhead box protein 3
OFC: Oral food challenge
OIT: Oral immunotherapy
SPT: Skin prick test
Treg: Regulatory T

response to the substance on subsequent encounters. Traditional subcutaneous immunotherapy with aqueous peanut extract was attempted but had an unacceptably high rate of systemic reactions, despite favorable challenge outcomes.¹⁴

In pilot studies, our group has shown that open-label peanut oral immunotherapy (OIT) was relatively safe when performed in a supervised medical setting by trained personnel¹⁵ and was associated with clinical desensitization for the majority of subjects completing more than 8 months of treatment.¹⁶ To establish the safety and efficacy of peanut OIT as an allergen-specific therapy for peanut allergy, we conducted the first randomized, double-blind, placebo-controlled study of OIT in children with peanut allergy. The primary endpoint was the amount of peanut protein ingested at food challenge by peanut OIT and placebo subjects after 1 year of treatment; in addition, we studied relevant immunologic mechanisms. We hypothesized that subjects receiving peanut OIT would be able to ingest more peanut protein than subjects receiving placebo.

METHODS

Subject recruitment

Subjects age 1 to 16 years were recruited from the allergy and immunology clinics at Arkansas Children's Hospital and Duke University Medical Center or surrounding community physician offices.

Subject selection

Children with a clinical history of reaction to peanut within 60 minutes of ingestion, a peanut CAP-FEIA >15 kU/L (Phadia AB; Pharmacia, Inc, Uppsala, Sweden) or >7 kU/L if a significant reaction occurred within 6 months of enrollment, and a positive skin prick test ([SPT] ≥ 3 mm of negative control) were enrolled. Subjects were excluded if they had a history of severe peanut anaphylaxis (hypoxia, hypotension, or neurologic compromise), moderate to severe persistent asthma, poorly controlled atopic dermatitis, oat allergy (because of the oat-based placebo), or inability to discontinue antihistamines for skin testing and food challenges.

Randomization

A randomization table was generated to assign subjects in a 2:1 ratio to receive peanut flour or placebo. Allocation was performed before enrollment and saved in a locked database accessible only by laboratory personnel to keep clinical staff and subjects unaware of upcoming assignments. Investigators, subjects, and families remained blind to the assigned intervention as well as all laboratory studies until completion of the food challenge.

Peanut and placebo flour and dosing

Premeasured peanut flour (from Partially Defatted Peanut Flour 12% Fat Light Roast; Golden Peanut Co, Alpharetta, Ga; 2 g flour = 1 g peanut protein) or placebo (toasted oat flour; Arrowhead Mills, Hereford, Tex) doses were mixed in a food vehicle of the subject's choosing and taken in 2 to 3 bites. Approximately 240 mg peanut protein equals 1 whole peanut.¹⁷ Intact allergen content in the soluble extract of roasted peanut flour is ~7% Ara h 2 and ~8% Ara h 1.

OIT protocol

While receiving the intervention (peanut flour or placebo), subjects were instructed to continue a strict peanut-free diet and to keep a diary of any missed doses or adverse symptoms. An epinephrine autoinjector was provided to all subjects. A member of the study team was available by pager and phone throughout the study.

Initial day escalation phase. The initial day escalation phase was performed on the research unit at each institution with appropriate emergency medications available. Dosing began at 0.1 mg peanut protein or placebo; doses were approximately doubled every 30 minutes until 6 mg was reached or the subject had symptoms. The highest tolerated dose was the starting dose for the build-up phase and was given on the research unit the following day. Subjects not tolerating at least 1.5 mg were withdrawn from the study.

Home dosing. Subjects were instructed to ingest each dose mixed in a vehicle food daily. On the basis of patterns observed during our open-label study,¹⁸ we advised subjects to hold dosing if febrile or ill and to take all doses on a full stomach. Dosing was resumed at home if the subject missed less than 3 daily doses; subjects returned for an observed dose if 3 to 5 doses were missed.

Build-up visits. Subjects returned every 2 weeks for approximately 44 weeks for dose escalations. Doses were increased by 50% to 100% until the 75-mg dose and were then increased by 25% to 33% until the 4000-mg maintenance dose was reached.

Maintenance phase. After reaching the maintenance dose of peanut flour or placebo, subjects ingested the dose daily for 1 month and then returned for the first oral food challenge (OFC) at week 48.

OFC

A double-blind, placebo-controlled food challenge was performed after 4 weeks of maintenance therapy. Before the OFC, subjects were asked to restrict the use of antihistamines, β -agonists, theophylline, and montelukast.¹⁶ All subjects were challenged to both peanut and oat flour in a blind manner. Challenges were administered by a nurse or physician who was also blind to the testing materials. The challenge consisted of peanut or oat flour given in increasing doses every 10 to 20 minutes up to a cumulative dose of 5000 mg protein.

Safety

The safety of peanut OIT compared with placebo was studied during the 4 phases of the protocol. Certain mild allergic side effects (ie, mild oral pruritus, contact urticaria) can be expected when administering OIT and do not require treatment or result in a change in the treatment plan. We defined clinically relevant side effects as those categorized as moderate or severe by study personnel (>1 on a symptom scale ranging from 0-3) and those requiring treatment with antihistamines or epinephrine. We calculated the rate of clinically relevant side effects during the initial day escalation, dose escalation visits, and OFC and the rate of epinephrine use during any phase of the study.

Purified peanut protein reagent

Peanut proteins were extracted from defatted peanut flour (Golden Peanut Co) in PBS, clarified by centrifugation (30,000g for 30 minutes), and sterilized by filtration. The protein concentration was determined by using the bicinchoninic acid assay (Pierce, Rockford, Ill).

Titration SPT

Titration SPT (1:20, 1:200, 1:2000, 1:20,000) with peanut extract (Greer Laboratories, Lenoir, NC) and saline and histamine controls were performed at enrollment and at the time of OFC. Tests to peanut were measured and followed at the same dilution that resulted in a wheal >5 mm at the baseline visit. Wheal size was calculated as the average of the largest diameter and the perpendicular midpoint diameter.

Assays for IgE, IgG, and IgG₄

Peanut-specific IgE, IgG, and IgG₄ levels were measured in serum by using the ImmunoCAP 100 instrument (Phadia AB) according to the manufacturer's instructions.

TABLE I. Baseline characteristics of subjects randomized to active or placebo intervention

Characteristic	Active	Placebo
Number	19	9
Age (mo), median (range)	84 (38-126)	69 (28-114)
Sex	9 Male, 10 female	9 Male
Race	18 White, 1 biracial	9 White
Subjects with asthma, n (%)	13 (68)	7 (78)
Subjects with atopic dermatitis, n (%)	14 (74)	4 (44)
Subjects with allergic rhinitis, n (%)	15 (79)	8 (89)
Subjects with other food allergy, n (%)	14 (74)	8 (89)
Baseline peanut IgE (kU/L), median (range)*	106 (31-685)	57 (20-188)
Baseline titrated SPT (mm), median (range)	7 (5.5-15)	7 (5.5-13)

* $P = .02$.

Secreted cytokine assays

Subjects with cultured PBMCs at baseline, 9 months, and the time of OFC underwent cytokine analysis. PBMCs were isolated from ~30 mL heparinized blood by using Ficoll-based density separation (LymphoH; Atlanta Biologicals, Lawrenceville, Ga). For cytokine assays, PBMCs were suspended in culture media (RPMI-1640; Mediatech) with 10% autologous plasma and were cultured at 37°C in 5% CO₂ humidified atmosphere for 72 hours in the presence of 200 µg/mL crude peanut extract or media alone. Culture supernatants were analyzed for a panel of 5 relevant cytokines (IL-5, IL-13, IL-10, IFN-γ, and TGF-β) by ELISA according to the manufacturer's instructions (R&D Systems, Minneapolis, Minn). Reported values were calculated by results of crude peanut extract stimulation minus culture media alone.

Regulatory T-cell analyses

Changes in the Tregulatory (Treg)-cell subset were analyzed in the 9 subjects enrolled at Duke University Medical Center who reached OFC. PBMCs were suspended in culture media as described and incubated for 7 days with crude peanut extract (200 µg/mL), tetanus toxoid (5 µg/mL; EMD Biosciences, Darmstadt, Germany), and medium alone (RPMI). Flow cytometry was performed, and CD4⁺CD25⁺ lymphocytes were gated for FoxP3^{intermediate} and FoxP3^{hi} signals by using FlowJo software (TreeStar, Ashland, Ore). In each FoxP3 gate, the percentage obtained after RPMI incubation was subtracted from crude peanut extract and tetanus toxoid values. The FoxP3^{hi}:FoxP3^{intermediate} ratio was calculated as recently described¹⁹ and plotted at baseline and OFC.

Ethics

Approval was obtained through each institution's institutional review board; procedures were in accordance with ethical standards of the responsible committee on human experimentation and the Helsinki Declaration of 1975, as revised in 1983. Written informed consent was obtained in accordance with each institution's ethics guidelines for research in children.

Statistical analysis

The Fisher exact test was used to compare baseline characteristics of active and placebo groups. Differences in the values over time compared with baseline were analyzed by using the Wilcoxon rank-sum test (Stata 10; StataCorp LP, College Station, Tex) on matched data, which was also used to test the primary hypothesis. In all analyses, P values <.05 were considered significant. The sample size target was 60 individuals, with random assignment to peanut and placebo of 2:1, and was designed to have 95% power to detect with a 2-sided 5% level test a difference between a 20% desensitization rate for

TABLE II. Safety profile: number of subjects requiring treatment with epinephrine

Study phase	Active	Placebo
Initial escalation day	2 of 19	0 of 9
Build-up visits	0	0
Home dosing	0	1 of 9
OFC	0 of 16	3 of 9

placebo-treated versus an 80% rate for peanut OIT-treated subjects. A predetermined analysis by the data safety monitoring board was to be done after their review of the initial OFC. Because of the significant difference in OFC outcomes, enrollment was stopped at the number of enrolled subjects.

RESULTS

Study population

Twenty-eight subjects were enrolled between March 2007 and December 2008 (Table I). No screened subjects were excluded because of severe systemic reactions to peanut. The median age at enrollment was 69 months (range, 28-126). The active treatment group (9 males, 10 females) had a median baseline IgE level of 104 kU/L (range, 31-685 kU/L); the placebo group (9 males) had a median baseline IgE level of 57 kU/L (range, 20-188 kU/L).

Initial day escalation

During the initial day escalation, 26 (93%) of 28 subjects reached the maximum cumulative dose of 12 mg study protein (2 subjects ingested 15 mg study protein because of a repeated dose). Nine (47%) of 19 peanut OIT subjects experienced clinically relevant side effects requiring antihistamine treatment. Of these, 2 also required treatment with epinephrine (Table II). Two peanut OIT subjects did not reach the 1.5-mg dose and were deemed initial day escalation failures. No placebo subjects had clinically relevant symptoms or required treatment.

Build-up doses

Peanut OIT subjects had clinically relevant symptoms after 1.2% of 407 buildup doses on the research unit. None required treatment with epinephrine or hospitalization. One peanut OIT subject withdrew from the study after the first dose escalation because of mild gastrointestinal symptoms precluding further dosing. No placebo subjects had clinically relevant symptoms with dose escalation visits.

Home doses

No peanut OIT subjects needed epinephrine with home doses; 1 placebo subject was given epinephrine at home for symptoms with a placebo dose (Table II). Sixteen of 19 subjects (84%) reached the goal maintenance dose of 4000 mg.

OFC

Peanut OIT subjects reached OFC after a median of 12.4 months on treatment (range, 11.3-16.3 months) versus 11.7 months for placebo-treated subjects (range, 11-13.8 months; $P = .07$). As shown in Fig 1, all peanut OIT subjects reaching OFC ($n = 16$) ingested the maximum cumulative dose of 5000

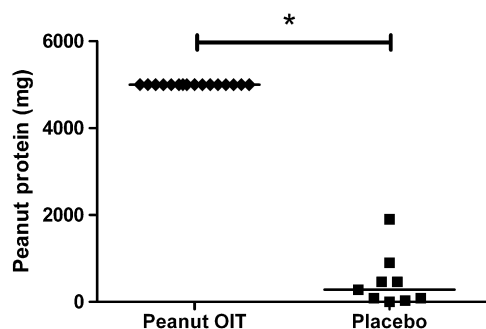


FIG 1. Cumulative amount of peanut protein ingested at OFC by peanut OIT and placebo subjects (* $P < .001$) after 12 months of therapy. Individual subjects are shown as *diamonds* (peanut OIT) or *squares* (placebo); lines designate median values.

mg (approximately 20 peanuts), whereas placebo subjects ($n = 9$) ingested a median cumulative dose of 280 mg (range, 0–1900 mg; $P < .001$). One peanut OIT subject had clinically relevant symptoms (mild upper respiratory symptoms and moderate urticaria) after completing the challenge and received antihistamine treatment. No peanut OIT subject required epinephrine or hospitalization (Table II). Eight placebo subjects had clinically relevant symptoms (1 had grade 1 objective gastrointestinal symptoms and oral pruritus), 3 requiring treatment with epinephrine (Table II). No placebo subjects required hospitalization.

Titrated SPTs

As shown in Fig 2, in the peanut OIT group, titrated SPT size decreased from a median of 7 mm (range, 5.5–15 mm) at baseline to 1.75 mm (range, 0–10 mm) at the time of OFC ($P < .001$). There was no significant change in SPT size in the placebo group; titrated SPT was 7 mm (range, 5.5–13 mm) at baseline and 4 mm (range, 0–12.5 mm) at OFC.

Peanut-specific serum IgE, IgG, IgG₄

The median baseline peanut IgE levels in the peanut OIT and placebo groups were 104 kU/L (range, 31–685 kU/L) and 57 kU/L (range, 20–188 kU/L), respectively ($P = .02$). In peanut OIT subjects, median peanut-specific IgE increased nearly 3-fold by 2 months (to 308 kU/L; $P < .01$) and was not significantly different from baseline at OFC (Fig 3, A); placebo subjects showed no changes. Peanut OIT subjects had significant increases in peanut-specific IgG at all time points (Fig 3, B). Peanut-specific IgG₄ showed a significant increase from baseline at all time points with peanut OIT and did not change with placebo (Fig 3, C).

Secreted cytokines

A panel of 5 cytokines was measured at baseline, at 9 months, and at the time of OFC in 8 peanut subjects and 9 placebo subjects who had cultured PBMCs at these time points. IL-5 and IL-13 significantly decreased from baseline in peanut OIT subjects at 9 months and OFC (Fig 4, A and B; $P < .03$). There was a transient increase in TGF- β levels in peanut OIT subjects at 9 months ($P = .03$; data not shown); levels returned to baseline at OFC. There was no change in IL-5, IL-13, or TGF- β in placebo-treated subjects. There was no significant change in IL-10 or IFN- γ in either peanut OIT or placebo subjects.

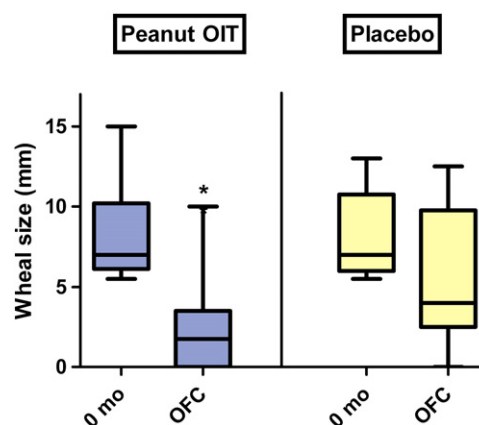


FIG 2. Titrated skin prick testing. Change in median wheal size from baseline to time of OFC in peanut OIT and placebo subjects (* $P < .001$). Boxes represent 25% to 75% quartiles; whiskers represent range. Lines designate median values.

Treg cells

Peanut OIT subjects had an increase from baseline in the ratio of FoxP3^{hi}: FoxP3^{intermediate} CD4⁺CD25⁺ Treg cells at the time of OFC (Fig 5, A; $P = .04$). Importantly, this change was not observed for the control antigen, tetanus toxoid. Placebo subjects had no change in Treg cells (Fig 5, B).

DISCUSSION

This is the first double-blind, placebo-controlled study of peanut OIT as a treatment for peanut allergy. By establishing the safety and efficacy of allergen-specific desensitization, these data support the feasibility of using peanut OIT as an interventional therapy. Sixteen of 19 subjects (84%) completed 1 year of peanut OIT treatment; 3 (16%) were unable to complete the protocol. All 16 reaching OFC completed the 5000-mg peanut protein challenge, ingesting approximately 20 peanuts; only 1 subject required antihistamine therapy. Subjects receiving placebo ingested a median cumulative dose of 280 mg, or approximately 1 peanut, before stopping the OFC because of allergic symptoms. Desensitization represents an important advance in the treatment of food allergy by increasing the threshold of the food antigen causing allergic symptoms. This degree of protection would likely prevent accidental peanut anaphylaxis, offering great benefit to affected patients and their families. Studies addressing the impact of peanut OIT on health-related quality of life are currently underway.^{20,21}

The immunologic changes during peanut OIT in antigen-specific immunoglobulins, mast cells, and T cells mirror those seen with traditional allergen immunotherapy and are similar to the natural development of tolerance to food allergens.²² In active subjects but not controls, peanut-specific IgE increased during the first year of OIT treatment but was not significantly different from baseline levels at OFC, whereas peanut-specific IgG and IgG₄ increased as early as 2 months into treatment and continued to rise throughout the first year. Titrated SPT size decreased by the time of OFC. Peanut OIT induced a shift in allergen-specific cytokine production away from a T_H2-type profile, with decreased IL-5 and IL-13 production. Peanut OIT subjects had an increased ratio of FoxP3^{hi}: FoxP3^{intermediate} CD4⁺CD25⁺ T cells at OFC, which may represent the induction of Treg cells important in suppressing

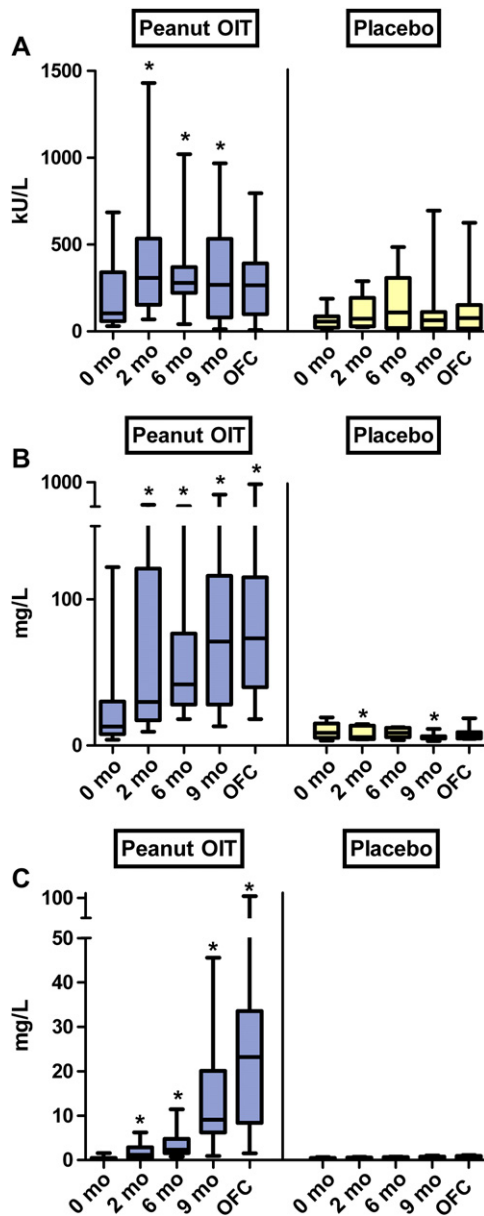


FIG 3. Changes in serum immunoglobulin levels during treatment with peanut OIT and placebo. **A**, Peanut-specific IgE ($*P \leq .01$). **B**, Peanut-specific IgG ($*P < .05$). **C**, Peanut-specific IgG₄ ($*P \leq .001$). Boxes represent 25% to 75% quartiles; whiskers represent range. Lines designate median values.

the allergic response. Allergen-specific Treg cells may play a role in the natural resolution of milk allergy²³; it is possible that the same immunosuppressive functions play a role in OIT. The exact mechanism of Treg-induced immunosuppression remains unknown. It is interesting that there was only a transient increase in blood TGF- β levels and no change in IL-10 levels; it is possible that blood cytokine levels do not reflect mucosal production or that mucosal Treg function differs from that seen in the periphery.

This study uses a rigorous study design to confirm and extend the findings seen in our open-label study¹⁶ and adds to the small body of literature of controlled interventional food allergy trials.^{10,24} It is unlikely that all subjects in the intervention group naturally outgrew their allergy given their history and baseline immunologic parameters. Furthermore, all placebo subjects

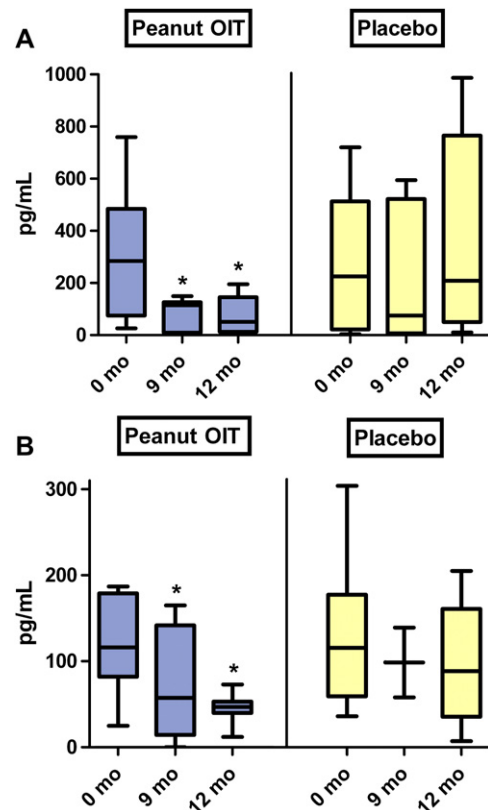


FIG 4. Changes in secreted cytokine responses for subjects receiving peanut OIT and placebo. PBMCs were cultured with peanut protein for 72 hours; cytokines were measured via ELISA. **A**, IL-5 ($*P \leq .02$). **B**, IL-13 ($*P \leq .03$).

reacted at low doses of peanut protein after approximately 1 year in the study; none demonstrated natural tolerance acquisition. The only other placebo-controlled study of OIT for food allergy found an increased amount of milk protein ingested at challenge as well as increased milk-specific IgG₄ levels in subjects receiving active treatment but not placebo.²⁵ Although a number of subjects receiving active treatment had changes in the endpoint titration SPT threshold, the median change did not reach statistical significance, and there was no change in milk-specific IgE, possibly because of methodologic differences (sample size, shorter study duration) or differing immune responses to different allergens.

This regimen was well tolerated, with peanut OIT subjects experiencing clinically relevant symptoms after only 1.2% of build-up doses. Importantly, no peanut OIT subjects required epinephrine treatment with dose escalation visits or home doses. During the open-label study, we observed certain patterns of allergic reactions with home dosing and were able to implement changes in this blind study.¹⁸

The strengths of this study include its placebo-controlled design, favorable safety profile, and convincing clinical desensitization, which occurs in parallel with biologically relevant immune modulation. However, there are also several important limitations to note. We use the term *desensitization* to signify a change in the amount of food antigen needed to cause allergic symptoms; this state is dependent on regular antigen exposure. In contrast, *tolerance* refers to long-term immunologic changes

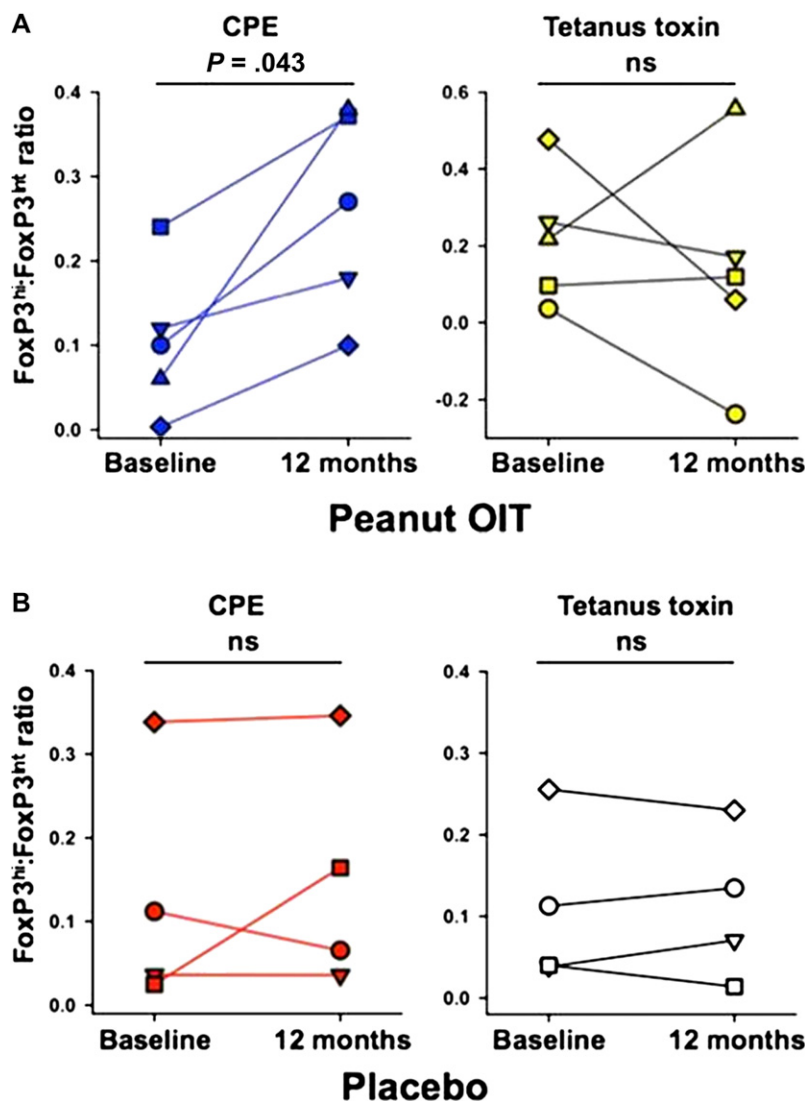


FIG 5. Change in FoxP3^{hi}:FoxP3^{intermediate} CD4⁺CD25⁺ T cells from baseline to time of OFC. PBMCs were stimulated with crude peanut extract and tetanus toxin for 7 days and then stained for Treg markers. Individual subjects are shown for peanut OIT (A) and placebo (B) groups. * $P = .04$. ns , Not significant.

associated with the ability to ingest a food without symptoms and without ongoing therapy. Desensitization is a worthwhile therapeutic goal in that it offers individuals freedom from the risk of accidental ingestion in everyday settings; achieving long-term clinical tolerance would allow safe food ingestion without ongoing therapy by inducing lasting immunologic changes. This report does not address the induction of tolerance, which requires longer-term follow-up; the subjects in this study continue to receive peanut protein, and these longer-term outcomes will be followed. In addition, baseline entry challenges are necessary to evaluate definitively the change in threshold dose with OIT treatment; future protocols will use challenges at study entry to define baseline allergen thresholds. The study's sample size is small, limiting the ability to generalize the results. Moreover, this protocol included only children, and further study is needed to evaluate the efficacy of OIT in adults with long-standing peanut allergy.

Peanut OIT is relatively safe under strict supervision; however, with current forms of OIT, as with other forms of immunotherapy, certain individuals are unable to endure associated side

effects.^{15,26} In this cohort, 3 subjects were unable to complete the initial day escalation or build-up dosing because of side effects. Further study may help identify the clinical and/or immunologic profiles of patients who are the best candidates for this therapy. Although many of our subjects had experienced systemic reactions to peanut before enrollment, we excluded patients with a history of severe anaphylaxis. This is an important limitation, because these severely affected patients may be more likely to seek treatment. Moreover, there remain numerous unanswered questions that must be addressed before OIT can be applied in widespread clinical use, including risks of OIT compared with avoidance, dosing regimen issues, patient selection, postdesensitization strategy, allocation of clinical resources, and reimbursement.²⁷

When performed by experienced investigators in an appropriate setting, peanut OIT is a safe, allergen-specific therapy effective in inducing desensitization and providing protection against accidental exposure with ongoing therapy. Immunologic changes suggest downregulation of the allergic response. Further

investigation of this promising intervention will address outstanding issues and continue to refine therapeutic protocols in the hope of offering an allergen-specific treatment option for food allergy.

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Key Messages

- After 1 year of treatment, subjects receiving peanut OIT were able to ingest a greater amount of peanut protein than those receiving placebo.
- Clinical efficacy was accompanied by the following peanut-specific immunologic changes: decreased SPT and T_H2 cytokine production and increased IgG₄ and Treg cells.
- These results demonstrate that peanut OIT induces desensitization and concurrent immune modulation. The current study continues and is evaluating the hypothesis that peanut OIT causes long-term immune tolerance.

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