STUDY POPULATION. The study included 74 patients ages 4–25 years with a peanut allergy, defined as physician-diagnosed or as the patient having a convincing clinical history of a peanut allergy, a positive result on a peanut skin prick test, or peanut-specific IgE and a positive entry oral food challenge (OFC) to 1044 mg of peanut protein or less. Children with a history of severe anaphylaxis were excluded.

METHODS. Participants were randomly assigned to double-blind peanut EPIT using Viaskin Peanut 100 μg (VP100) or 250 μg (VP250) or a placebo patch. The patch was placed on the back or upper arm daily for increasing lengths of time, up to 24 hours per day. The primary outcome, or treatment success, was defined as passing a 5044-mg peanut protein OFC or demonstrating a 10-fold or greater increase in the consumed dose from baseline after 52 weeks of treatment. Secondary outcomes included adverse reactions, adherence, effects of age and dose on outcomes, and immunologic changes.

RESULTS. Twelve percent of the placebo group, 46% of the VP100 group, and 48% of the VP250 group met the primary endpoint, though none in the treatment group passed the 52-week OFC. The median change of successfully consumed peanut protein was 0 mg of protein in the placebo group, 43 mg in the VP100 group, and 130 mg in the VP250 group. Children 11 years or younger were more likely to achieve treatment success. Adverse reactions, most commonly mild patch-site reactions, were more common in the treatment groups (80% of both VP100 and VP250 doses vs 14% of placebo). No epinephrine was used for treatment of dose reactions. Peanut-specific IgG_4 levels and IgG_4/IgE ratios increased in both treatment groups when compared with the placebo group, though no change was seen for peanut-specific IgE levels or skin test size among groups.

CONCLUSIONS. Peanut EPIT resulted in a modest but significant increase in the successfully consumed dose of peanut protein after 1 year of treatment with both the VP100 and VP250 doses when compared with placebo. Younger participants achieved greater treatment success. Immune modulation consistent with other forms of food immunotherapy was noted. Local patch-site reactions were common, but there were no serious reactions. Adherence to therapy was high.

REVIEWER COMMENTS. This is the first trial to comprehensively evaluate EPIT for the treatment of peanut allergy, introducing another prospective treatment option for food allergy. Though clinical and immunologic responses in this study were modest, the safety profile and adherence rate were favorable. Future studies will investigate whether the treatment benefit will become more robust with longer duration of treatment and continue to refine the target patient population who may benefit most from EPIT.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2017–2475VV

Sheeba Cherian Kunnel, MD
Pooja Varshney, MD
Austin, TX

Early Oral Immunotherapy in Peanut-Allergic Preschool Children is Safe and Highly Effective

Vickery BP, Berglund JP, Burk CM, et al. *J Allergy Clin Immunol*. 2017;139(1):173–181.e8

PURPOSE OF THE STUDY. To evaluate the efficacy, safety, and feasibility of early oral immunotherapy (E-OIT) for treatment of peanut-allergic children.

STUDY POPULATION. The study included 40 infants and preschool children (9–36 months of age) with either a known peanut allergy or peanut sensitization (peanut-specific immunoglobulin E (IgE) $>5kU_A/L$ but no history of reaction). Matched data from a control cohort of 154 participants was retrospectively obtained from a database at Johns Hopkins and compared with study participants.

METHODS. In this randomized active treatment study, each enrolled subject underwent an open oral food challenge to 4 g of peanut protein at study entry. Subjects with IgE-mediated allergic reactions were randomized 1:1 to receive either low-dose (300 mg/d) or high-dose (3000 mg/d) blinded maintenance dosing of peanut protein. Each participant had an initial-day escalation and an ~42-week buildup phase to the goal maintenance dose. Participants in the low-dose arm consumed their peanut protein product mixed with oat flour to maintain blinding. After the study subjects either met specific criteria or had undergone 36 months of maintenance dosing, subjects underwent two double-blinded, placebo-controlled food challenges to assess desensitization and sustained unresponsiveness 4 weeks after cessation of E-OIT. After passing both food challenges, subjects consumed one additional serving of peanut openly and, if tolerated, were allowed to reintroduce peanut ad lib. Peanut-specific IgE levels were followed over time.

RESULTS. Thirty-two subjects had evaluable outcomes, 81% were desensitized (low dose: 76%, high dose: 85%), and 78% achieved 4-SU (low dose: 85%, high dose: 76%, $P = .43$) over a median treatment period of 29 months. The median (IQR) peanut-specific IgE levels declined significantly in the study group (1.6 kU_A/L [0.5–4.9 kU_A/L]) while increasing in the matched control group (57.4 kU_A/L [9–101 kU_A/L]). The proportion of the control group who successfully introduced peanut in their diet was 4%, compared with 78% in the study group (RR, 19.42; 95% CI, 8.7–43.7; $P < .001$). E-OIT was overall safe and well tolerated with no serious

adverse events. Although adverse events were noted in 95% of subjects, all were of mild to moderate severity and only required an antihistamine for treatment.

CONCLUSION. Early oral immunotherapy with peanut protein at both high- and low-maintenance dosing is very effective for inducing sustained unresponsiveness and accelerating the introduction of peanut in the diet of preschool, peanut-allergic children when compared with a natural history control cohort of peanut-allergic children. Furthermore, this study demonstrated that E-OIT is relatively safe, with no serious adverse events noted in this young age group.

REVIEWER COMMENTS. This is the first study to demonstrate effectiveness and safety of OIT in young children, suggesting an advantageous window of time to induce immunomodulation and impact allergic status in young children. Results from ongoing and future studies with placebo-controlled treatment in young children will provide additional information about the potential benefit of early intervention for peanut allergy using oral immunotherapy.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2017–2475WW

Annette Carlisle, MD
Stacie M. Jones, MD
Little Rock, AR

Novel Baseline Predictors of Adverse Events During Oral Immunotherapy in Children With Peanut Allergy

Virkud YV, Burks AW, Steele PH, et al. *J Allergy Clin Immunol*. 2017;139(3):882.e5–888.e5

PURPOSE OF THE STUDY. To characterize the frequency of adverse events (AEs) associated with peanut oral immunotherapy (OIT) and to identify baseline characteristics that predict higher risk of AEs.

STUDY POPULATION. This retrospective cohort analysis included 104 pediatric subjects enrolled in 3 peanut OIT trials. All participants had a positive peanut skin test (SPT); the majority had an elevated peanut-specific IgE level and other allergic diseases.

METHODS. Safety data were collected from symptom records during dose escalation at the research unit, symptom diaries of home AEs, and parental report of home AEs. All events considered likely related to OIT by study investigators at the time of occurrence were studied. Statistical models were used to identify baseline predictors of AEs.

RESULTS. Eighty percent of subjects experienced at least 1 AE. Eighty-five percent of AEs were mild, and 15% were moderate. Ten percent of AEs were classified as systemic. The AE rate was higher in the buildup phase than the maintenance phase. More than 90% of AEs occurred at home. AEs involved the skin, respiratory system, and GI tract. Almost half of the subjects experienced GI symptoms. Nearly 13% withdrew from OIT because of AEs, most commonly because of new-onset GI symptoms. Adjusting for confounding variables, allergic rhinitis (AR) and peanut SPT size were significant predictors of the overall rate of AEs. AR was the only predictor of systemic AEs and was associated with the seasonality of AEs. Peanut SPT size was the only predictor of GI AEs. Asthma was associated with increased AEs during the maintenance phase only. Sixty-one percent of subjects received treatment with antihistamines, steroids, albuterol, or epinephrine; 12% received epinephrine. Eighty-five percent of systemic AEs were not treated with epinephrine.

CONCLUSIONS. Peanut OIT is associated with frequent, though usually mild, AEs. Persistent GI symptoms are the most common cause of OIT dropout. AR and peanut SPT size are significant predictors of systemic and GI AEs, respectively. Knowledge gaps surrounding epinephrine use exist, even in highly motivated research populations.

REVIEWER COMMENTS. This is the largest safety analysis to date of peanut OIT in a controlled research setting. The study confirms a high rate of typically mild AEs and identifies peanut SPT size as a useful predictor of GI AEs, which are confirmed as the most common reason for dropout. The novel finding of AR as a risk factor for AEs will inform future investigation. While OIT is a promising therapy, this study highlights the need for further examination of its risk-to-benefit ratio before widespread clinical use.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2017–2475XX

Kathryn Neupert, MD
Pooja Varshney, MD
Austin, TX

Extended Boiling of Peanut Progressively Reduces IgE Allergenicity While Retaining T Cell Reactivity

Tao B, Bernardo K, Eldi P, et al. *Clin Exp Allergy*. 2016; 46(7):1004–1014

PURPOSE OF THE STUDY. To evaluate the impact of extended boiling on peanut allergenicity and T cell reactivity.

STUDY POPULATION. Blood samples were collected from 10 peanut-allergic children ages 8 to 14 years with peanut-specific IgE ranging from 91.8 to >100 kU/L. Skin prick tests using boiled peanut extracts were performed on 20 known peanut-allergic children ages 2 to 16 years. Blood samples were collected for peanut antigen-specific T cell assays from 3 peanut-allergic patients and 3 nonallergic volunteer controls.

METHODS. Raw peanuts were boiled for 30 minutes, 1 hour, 2 hours, 4 hours, and 12 hours in deionized water. After

Early Oral Immunotherapy in Peanut-Allergic Preschool Children is Safe and Highly Effective

Annette Carlisle and Stacie M. Jones

Pediatrics 2017;140;S200
DOI: 10.1542/peds.2017-2475WW

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Early Oral Immunotherapy in Peanut-Allergic Preschool Children is Safe and Highly Effective

Annette Carlisle and Stacie M. Jones

Pediatrics 2017;140;S200
DOI: 10.1542/peds.2017-2475WW