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.

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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.

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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

dehydration, boiled and raw peanuts were ground, defatted in acetone, agitated, centrifuged, and air dried for 24 hours. The resultant pellet was resolubilized in 5 volumes of phosphate-buffered solution, and both the peanut extract and the leachate-containing solubilized peanut proteins were sterilized and retained. SDS-PAGE, Western blot, two-dimensional electrophoresis, IgE-inhibition ELISA, mass spectrometry, and skin prick testing were used to characterize changes to peanut allergens and human IgE reactivity associated with progressive boiling. T cell responses to raw and boiled peanut extracts were determined by proliferation of CD4+/CD25+/CD134+ T cells in peanut-allergic and nonallergic patient blood samples.

RESULTS. Extended boiling caused increasing fragmentation of peanut proteins into lower molecular weight polypeptides, denaturing of conformational epitopes, and transference of proteins to the leachate. Compared with the raw peanut extract, eightfold more 2-hour boiled peanut extract and 19-fold more 12-hour boiled peanut extract were required to achieve 50% inhibition of IgE by inhibition ELISA. Boiling increased the number of unique allergen peptides apparent via mass spectrometry in the boiled peanuts by more than fivefold at 2 hours and by 42-fold at 12 hours. As compared with unboiled raw peanut extract, skin prick testing demonstrated a significant reduction in wheal size to 55% for the 2-hour boiled peanut extracts and to 36% for the 4-hour boiled peanut extracts. Raw peanuts and 2-hour and 12-hour boiled peanut extracts were equivalent in their ability to stimulate T cell activation and proliferation.

CONCLUSIONS. Progressive reduction in peanut allergenicity with extended boiling does not affect T cell reactivity. Boiled peanuts may be a candidate for future peanut oral immunotherapy.

REVIEWER COMMENTS. Oral immunotherapy using raw peanuts, roasted peanuts, or peanut oil is associated with high rates of adverse events and is therefore not currently recommended for routine clinical practice. A product able to initiate peanut desensitization with fewer adverse events is desirable. Previous investigations of boiled peanut products have studied peanuts boiled for no longer than 1 hour. The current study demonstrates that boiling peanuts for at least 2 hours is required to significantly reduce the allergenicity of Ara h 2, which is stabilized by the presence of 4 disulphide bonds. Extensively boiled peanuts may be an attractive option for future oral immunotherapy secondary to decreased IgE reactivity, with retained peptides capable of stimulating T cell activity.

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Oral Immunotherapy With Low Allergenic Hydrolyzed Egg in Egg Allergic Children

Giavi S, Vissers YM, Muraro A, et al. *Allergy*. 2016;71 (11):1575–1584

PURPOSE OF THE STUDY. Egg allergy is 1 of the most common food allergies in children. This study aims to investigate a method to desensitize egg-allergic patients so that they can develop long-lasting oral tolerance to egg proteins.

STUDY POPULATION. Twenty-nine egg-allergic patients (ages 1–5.5 years) from 3 study sites in Europe (Greece, Switzerland, and Italy). These patients had positive testing to egg via either in vitro or skin prick testing as well as had a reaction during an oral food challenge.

METHODS. This was a double-blind placebo-controlled randomized study using well-characterized, low-allergenic hydrolyzed egg for oral immunotherapy. Subjects were randomized 1:1 to receive 9 ± 1 g study product or placebo daily for 6 months. An oral food challenge was conducted at the end of the study. Immunologic parameters were assessed at baseline and at the end of the study.

RESULTS. Upon completion of the study, the rate of success in an oral food challenge to a boiled egg was no different between treatment groups (36% active vs 21% placebo, $P = .66$). There was no significant difference observed for egg-specific IgE levels, but a significant increase in egg-specific IgG_4 was seen in the study group.

CONCLUSIONS. The well-characterized, low-allergenic hydrolyzed egg product was found to be safe for use in children with egg allergy. A longer treatment duration and/or higher dose may be needed for clinical efficacy.

REVIEWER COMMENTS. This study offers a potentially safer product for use in oral immunotherapy to egg because there were no differences in type or severity of adverse effects between treatment groups. It is conceivable that with a longer study period and perhaps dosage adjustments, clinical improvement may be seen. Given the rate of food allergies and the burden of daily management on families, it will be important to see what continued investigation in this topic will bring to light because it may help treat the allergy and assuage parental fears.

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Safety and Efficacy of Low-Dose Oral Immunotherapy for Hen's Egg Allergy in Children

Yanagida N, Sato S, Asaumi T, Nagakura K, Ogura K, Ebisawa M. *Int Arch Allergy Immunol*. 2016;171(3–4):265–268

PURPOSE OF THE STUDY. The ideal dose for safe and effective oral immunotherapy (OIT) is unknown. The goal of this

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