reaction, 70.7% had experienced anaphylaxis, 26% had a peanut-specific immunoglobulin E (PSIgE) concentration of >100 kU/mL, and 9.6% had a positive peanut challenge result within 2 years of inception of POIT. No patient was excluded on the basis of severity of previous reaction(s) or PSIgE concentration. Patients with a history of eosinophilic esophagitis or gastroenteritis were excluded.

METHODS: The treatment protocol began with 2.5 μg of peanut protein. Dose increases were administered under direct observation. Patients reached a target dose of 3000 mg of peanut protein, underwent a 6000-mg challenge, and then began a 2000-mg maintenance dose administered at home 1 to 2 times per day for a minimum of 3 years. The treatment team made dose adjustments and decisions regarding discontinuation of therapy on the basis of collaborative clinical judgment. Patients and caregivers were instructed to report any adverse reactions more significant than transient, self-limited oral pruritis or abdominal discomfort.

RESULTS: A total of 214 of 270 patients (79%) completed POIT dose escalation. Age ($P < .001$) and PSIgE ($P < .001$) correlated inversely with completion of dose escalation. For each year increase in patient age after 5, there was a 17% decrease in the odds ratio of reaching the escalation target ($P < .001$). One hundred epinephrine-treated reactions occurred in 63 patients (23%) during escalation. Intermittent asthma and higher PSIgE levels increased the risk of epinephrine-treated reactions ($P = .035$ and .019, respectively). Eosinophilic esophagitis–like oral immunotherapy–related syndrome occurred in 37 patients (13.7%). Intermittent asthma and higher PSIgE levels increased the risk of eosinophilic esophagitis–like oral immunotherapy–related syndrome ($P = .014$ and $<.001$, respectively). After 3 years of maintenance treatment, 14 patients were able to achieve sustained peanut unresponsiveness, defined as tolerance of 6000 mg of peanut protein after avoiding peanut for 30 days. The best predictors of sustained unresponsiveness were a pretreatment PSIgE level <20 kU/L and a prechallenge PSIgE level <1 kU/L.

CONCLUSIONS: In an allergy office practice, 79% of patients were able to complete a POIT desensitization protocol and maintain a desensitized state with daily peanut dosing.

REVIEWER COMMENTS: This study demonstrates that patients can achieve successful peanut desensitization despite a history of previous reaction(s) or markedly elevated PSIgE levels. Epinephrine-treated reactions did occur during POIT, demonstrating that risk of significant allergic reactions was not eliminated. Reduced likelihood of achieving the target dose with increasing age makes early intervention attractive. Additional future studies are necessary to improve risk assessment and identification of patients likely to achieve sustained unresponsiveness.

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Oral Immunotherapy for Peanut Allergy (PACE): A Systematic Review and Meta–analysis of Efficacy and Safety

Chu DK, Wood RA, French S, et al. *Lancet*. 2019;393(10187):2222–2232

PURPOSE OF THE STUDY: To systematically review the efficacy and safety of peanut oral immunotherapy (OIT) compared with allergen avoidance or placebo OIT for peanut allergy.

STUDY POPULATION: The population included individuals with peanut allergy (61% male, 39% female), the majority of whom were children (median age: 8.7 years; interquartile range [IQR]: 5.9–11.2 years) participating in peanut OIT trials in North America, Australia, and Western Europe.

METHODS: This systematic review and meta-analysis included a comprehensive search of international health care databases from the United States, Latin America, Europe, and China through December 2018. Authors performed searches for randomized controlled trials comparing peanut OIT to no OIT for the treatment of peanut allergy. The authors screened studies, extracted data, assessed risk of bias, and assessed quality of evidence by the Grading of Recommendations Assessment, Development, and Evaluation approach. The main outcomes included treatment efficacy (ie, proportion of patients passing an oral food challenge), anaphylaxis, allergic or adverse reactions, epinephrine use, and quality of life.

RESULTS: Twelve randomized controlled trials were included, with 1041 participants in total undergoing peanut OIT for a median follow-up of 1.0 year (IQR: 0.8–1.4), achieving a median target dose of 2000 mg of peanut protein (IQR: 375–4000). Passing a supervised, in-clinic oral food challenge was more likely in the OIT group. Subjects undergoing peanut OIT had increased anaphylaxis risk (risk ratio: 3.12 [95% confidence interval (CI): 1.76–5.55]), anaphylaxis frequency (incidence rate ratio: 2.72 [95% CI: 1.57–4.72]), and epinephrine use (risk ratio: 2.21 [95% CI: 1.27–3.83]). Peanut OIT increased serious adverse events and nonanaphylactic reactions. These findings were irrespective of OIT protocol, proprietary formulation or not, and phase of OIT (build-up versus maintenance). Quality of life was not different between groups.

CONCLUSIONS: High-quality evidence shows that current peanut OIT regimens effectively achieve a modest level of desensitization but clinically result in a net increase in anaphylaxis and other allergic reactions compared with avoidance or placebo, rather than preventing them, as intended. These data support the need for improved food allergy treatment approaches with an enhanced safety profile.

REVIEWER COMMENTS: Hesitancy to implement OIT in routine clinical practice centers around concerns for safety, standardization of approach, practicality of long-term therapy maintenance, and identification of patients who will respond best with the fewest side effects. Although most adverse effects from OIT are mild and do not prevent patients from continuing therapy, the potential for life-threatening anaphylaxis exists. Despite the safety concerns outlined in this report, OIT is being offered in some clinical practices and is expected be available on a larger scale in the near future. It is important to remember that OIT may not be the best fit for many food-allergic patients, and as we near the likely acceptance of a US Food and Drug Administration–approved peanut OIT product, patients will seek advice from their pediatrician before talking to an allergist to help them navigate the pros and cons of interventional therapy versus the traditional approach of maintaining strict allergen avoidance. Salient points for the pediatrician to remember include the following. (1) OIT and all other products currently under investigation for treatment of food allergy provide benefit while on therapy but do not appear to induce sustained remission for the majority of allergic patients. (2) There are no surrogate biomarkers to identify which patients will receive the greatest benefit with the fewest side effects. (3) Anaphylaxis while on therapy is a potential side effect, and patients must continue to carry autoinjectable epinephrine at all times. Shared decision-making and an open and honest discussion with families considering therapeutic options are necessary in providing comprehensive care of our patients with food allergy and their families.

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Peanut Gastrointestinal Delivery Oral Immunotherapy in Adolescents: Results of the Build–up Phase of a Randomized, Double–Blind, Placebo-Controlled Trial (PITA Study)

Fauquert JL, Michaud E, Pereira B, et al; PITA Group. *Clin Exp Allergy*. 2018;48(7):862–874

PURPOSE OF THE STUDY: To assess the efficacy and safety using a new approach to oral immunotherapy in which high-risk peanut-allergic adolescents ingested sealed capsules of incrementally increasing amounts of peanut protein. In most published studies, peanut is administered in a vehicle food. The authors hypothesized that bypassing the upper digestive tract could improve efficacy because the lower digestive tract, the main anatomic site of oral tolerance, would be targeted, and sealed capsules would circumvent taste aversion.

STUDY POPULATION: Adolescents with peanut allergy were recruited for the study. Inclusion criteria included having a clinical reaction within 60 minutes after ingestion of peanut and demonstration of sensitization either by skin prick test (wheal >3 mm) or serum immunoglobulin E >12 IU/mL for peanut or >5.8 IU/mL for Ara h2 peanut component. Exclusion criteria included a teenager's history of severe anaphylaxis requiring ICU support; severe persistent asthma; poorly controlled atopic dermatitis; concomitant severe food allergy to egg, milk, nuts, or sunflower seed; and/or inability to manage a severe allergic reaction. All patients underwent an initial double-blind, placebo-controlled food challenge (DBPCFC) with sealed capsules containing peanut protein; to be included in the study, the adolescent had to have a convincing objective reaction occurring after a cumulate intake of >20 and ≤400 mg of peanut protein.

METHODS: Patients were randomly assigned 2:1 to active treatment (peanut) or placebo (sunflower). Patients ingested a daily treatment dose of peanut protein or placebo via sealed gelatin capsules starting at 2 mg; doses were incrementally increased every 2 weeks up to 400 mg over a 24-week period. A second DBPCFC was performed at the end of the build-up phase. Cumulative ingestion of >400 mg of peanut protein without symptoms was the definition of desensitization.

RESULTS: Fifty-one patients were screened, 21 patients were excluded because they tolerated 400 mg of peanut protein at the initial DBPCFC, and 30 patients were enrolled because they had a positive initial DBPCFC. Of these 30 enrolled patients, 21 were allocated to the peanut group and 9 were allocated to the placebo group. Two patients assigned to the peanut group withdrew from the study because of side effects; 1 of these patients experienced a severe adverse event (AE) but had inadvertently ingested twice the investigated amount. An additional 2 patients in the peanut group were unable to increase their intake threshold >400 mg but did increase their threshold level six- and sevenfold, respectively. Unresponsiveness to >400 mg of peanut protein was achieved in 17 of 21 (81%) patients with peanut allergy. Only 1 of 9 patients in the placebo group achieved this level of unresponsiveness. The number of patients experiencing AEs was not different between the 2 groups, but in the treated group, the number of AEs per patient was higher and AEs were more severe. Digestive AEs

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