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.

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

Karla L. Davis, MD
Fort Eustis, VA

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.

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

Samata Kamireddy, MD
Ricardo Sorensen, MD
New Orleans, LA

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

study was to investigate the efficacy and safety of low-dose OIT with approximately 1/32 of the volume of a whole egg.

STUDY POPULATION. Thirty-three children (aged ≥5 years) with egg allergies confirmed by oral food challenge (OFC) against 1/32 of a heated whole egg (194 mg of egg protein) were enrolled. Twenty-one children were enrolled in the OIT group and 12 in the control group.

METHODS. Children in the OIT group were admitted to the hospital for 5 days of buildup, and then at home, this group was encouraged to consume 62 to 194 mg of egg protein in scrambled form once a day. The amount of egg eaten, severity of provoked symptoms, and treatments administered were recorded in a diary. Egg consumption was completely absent in the control group. Twelve months later, the daily intake of egg ceased for 2 weeks, and an open OFC was performed on up to one-half of a whole egg. There were no significant differences between the groups in terms of subject background.

RESULTS. The proportion of subjects showing sustained unresponsiveness to 1/32 of a whole egg was 71.4% (15 of 21) in the OIT group and 0% (0 of 12) in the control group ($P < .001$). Subjects exhibiting sustained unresponsiveness to one-half of a whole egg were 33.3% (7 of 21) and 0% (0 of 12) in the OIT and control groups, respectively ($P = .032$). Compared with baseline levels, egg white– and ovomucoid-specific allergic markers were significantly different in the OIT group but not the control group. Adverse allergic reactions were infrequent, and most symptoms were classified as Grade 1 (mild). There were no Grade 3 (severe) symptoms reported. No subjects withdrew from the study, no epinephrine was used, and no emergency department visits occurred.

CONCLUSIONS. This study demonstrates that low-dose egg OIT may be safe and effective in a high-risk egg-allergic population, inducing both immunologic changes and sustained unresponsiveness to low doses and higher doses of egg. In addition, most adverse reactions were mild, no severe symptoms were reported, no epinephrine was used, and there were no emergency department visits.

REVIEWER COMMENTS. One of the major concerns with traditional OIT to foods is the amount, frequency, and severity of adverse allergic reactions, often causing significant subject withdrawal from these studies. This study demonstrates that using a lower dose of OIT is potentially safer. It also demonstrated effectiveness at inducing sustained unresponsiveness to both a low dose and a higher dose of egg protein. There are several limitations to the study, the first being this was a nonrandomized, open-labeled trial with a small sample size. Also, sustained unresponsiveness was only measured 2 weeks after stopping therapy, whereas most traditional studies use 4 or 6 weeks. Nevertheless, this could prompt future randomized controlled trials examining the safety and effectiveness of low-dose OIT.

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

Jonathan A. Hemler, MD
Nashville, TN

Ondansetron in Acute Food Protein-Induced Enterocolitis Syndrome, A Retrospective Case-Control Study

Miceli Sopo S, Bersani G, Monaco S, et al. *Allergy*. 2017; 72(4):545–551

PURPOSE OF THE STUDY. This study looked at the effectiveness of parenteral ondansetron in resolving acute symptoms of food protein–induced enterocolitis syndrome (FPIES).

STUDY POPULATION. This study examined patients aged 4 months to 14 years with a positive oral food challenge (OFC) for FPIES.

METHODS. This was a retrospective case series of OFCs done to either definitively diagnose FPIES or to assess for the resolution of FPIES. Positive challenges were defined as those that induced a reaction of vomiting within 0.5–6 hours of ingestion without cutaneous or respiratory symptoms suggestive of an IgE-mediated reaction. Treatment was categorized as traditional (normal saline IV bolus and methylprednisolone), ondansetron, or no therapy. Therapeutic success was defined as cessation of vomiting.

RESULTS. Sixty-six patients were included; 37 received ondansetron, 14 received traditional therapy, and 15 received no therapy. Nineteen percent of children in the ondansetron group continued to vomit compared with 93% in the traditional therapy group.

CONCLUSIONS. Parenteral ondansetron is significantly more effective than traditional therapy in resolving symptoms of FPIES. The findings suggest an effective treatment of vomiting in positive FPIES OFCs and allow for more confidence in performing OFCs.

REVIEWER COMMENTS. Food protein–induced enterocolitis is a non-IgE–mediated allergic disease of early childhood characterized by repetitive, profuse vomiting episodes and presenting within 1 to 4 hours of ingesting a triggering food. Cow's milk, soy, grains, egg, and fish are among the most common triggers. The diagnosis is primarily made through clinical history. While the pathophysiologic mechanism of the disease is not completely known, this study confirms prior research that ondansetron plays an important role in terminating episodes of FPIES reactions. The diagnosis of FPIES should be considered among patients with recurrent vomiting from triggering foods. Ondansetron can be used as a first-line therapy in the treatment of FPIES episodes

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Pediatrics 2017;140;S202
DOI: 10.1542/peds.2017-2475AAA

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Pediatrics 2017;140;S202
DOI: 10.1542/peds.2017-2475AAA