Two cases of anaphylaxis caused by perilla seed

To the Editor:

Perilla seed (*Perilla frutescens*) is one of the most popular spices in Asia, including Korea. Several *in vivo* and *in vitro* studies have demonstrated that perilla can suppress IgE-mediated responses, and no previous cases of allergic reactions or anaphylaxis induced by the perilla seed have been reported.

We report 2 cases of anaphylaxis caused by perilla seeds in which IgE-mediated mechanisms were suggested. Before the study, the patients gave full informed consent, and the local ethics committee approved the entire protocol. Both patients presented with generalized urticaria, wheezing, dyspnea, and dizziness immediately after ingesting food containing perilla seeds. The clinical characteristics of these 2 subjects are summarized in Table I. Both patients had atopy and showed positive responses to common inhalant allergens, including house dust mite, following a skin prick test. In addition, both patients had had allergic rhinitis and asthma for several years.

A skin prick test administered using perilla extracts (10 mg/mL) resulted in a strong positive response, whereas none of the 10 nonatopic healthy control subjects had positive responses. To confirm the causal relationship, an open food challenge test with perilla seeds (500 mg) was performed in both subjects, and immediate onset of severe allergic symptoms such as urticaria, dyspnea, severe facial angioedema, and dizziness with laryngeal edema were noted. These conditions improved with the administration of epinephrine, methylprednisolone, and antihistamine.

To investigate the pathogenic mechanism involved, serum specific antibodies to perilla extracts were measured using ELISA, and high serum-specific IgE and IgG4 antibody titers were detected in the patients’ sera compared with the titers in sera of 20 nonatopic healthy controls. To evaluate cross-reactivity, ELISA inhibition tests with sesame (*Sesamum indicum*), a very widely used spice, and house dust mite, an allergen commonly causing sensitivity in Korea, were performed. Significant dose-dependent inhibitions were noted with addition of perilla extracts, whereas no inhibition was seen with sesame or house dust mite extracts (data not shown).

Furthermore, IgE immunoblot analysis of the patients’ sera identified 1 IgE-binding component with a molecular weight of 21 kd (Fig 1).

![Fig 1](https://example.com/f1.png)

The identification of new food allergens is important because food allergy is a leading cause of anaphylaxis. Since perilla and sesame seeds first began to be used as major food additives in Asia, several cases of immediate hypersensitivity to sesame have been reported. However, the cases reported here are the first documented cases of perilla seed–induced anaphylaxis, and sensitivity arises mainly via the oral route.

The ability of sesame-derived protein and oil components to trigger IgE antibody–mediated immediate hypersensitivity and delayed hypersensitivity via cell-mediated immune responses has been demonstrated previously. In this study, 2 patients showed immediate responses to perilla seed on an oral challenge test and had positive skin prick tests. In addition, high serum-specific IgE and 1 IgE-binding component were noted, indicating that perilla seed ingestion can induce severe IgE-mediated allergic symptoms. Moreover, the patients had higher serum-specific IgG4 antibody titers than healthy normal controls. Further observations are needed to evaluate the clinical relevance of this antibody. Finally, ELISA inhibition results suggest that potential cross-reactivity with sesame extracts was very low. In conclusion, we have identified a new food allergen, perilla seed, in 2 patients.
with anaphylaxis in which an IgE-mediated response appears to be the pathogenic mechanism.

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Diagnostic accuracy of skin prick testing in children with tree nut allergy

To the Editor:

We read with interest the article by Fleischer et al1 on the natural history of tree nut allergy, which demonstrated how allergists could be guided in selecting the appropriate timing for tree nut challenges based on predictive decision points for tree nut--specific serum IgE. However, allergists in Australia,2 Britain,3 and France,4 among others, often rely on skin prick testing (SPT) in the diagnosis of food allergy. We would therefore like to share our experience in defining cutoff values for SPT wheal diameters that predict positive challenge outcomes to tree nuts and sesame. We have also included previously published data for peanut because this allergy commonly occurs in children and adults with tree nut allergy.

We performed an analysis of the computerized records of all patients who underwent SPT and challenges to peanut, tree nuts, and/or sesame between 1995 and 2005 at a university-affiliated children’s allergy center. SPTs to cashew, hazelnut, walnut, pecan, Brazil nut, and almond were performed using a single-lancet technique with commercial allergen extracts (Dome-Hollister-Stier, Spokane, Wash).5 Testing for pistachio nut and sesame seed (tahini) was performed by the prick-to-prick technique with fresh foods.6 Histamine (1 mg/mL) and a negative control solution were used for internal validation. SPTs were applied on the back of infants or the forearm of older children. The SPT wheal diameter (mm) to histamine was measured at 10 minutes and to allergens at 15 minutes after application. Irregular shapes were recorded as the mean of 2 perpendicular diameters. The SPTs were analyzed against formal oral food challenges performed within 3 months of skin testing. The challenge procedure for tree nuts and sesame was adapted from our previously described method for peanut.7 In brief, 1/8 to 1/4 teaspoon increments of finely ground unsalted nuts were administered at intervals of 20 to 30 minutes, as tolerated, until a total dose of 20 g was reached. Double-blind, placebo-controlled challenges were performed only if the open challenge was inconclusive. A negative challenge outcome was reviewed by telephone survey on day 7 and a clinical assessment on day 28. On day 7, a standard set of questions was asked to ensure the compliance with the challenge protocol and to verify any late symptoms. On day 28, patients were assessed as to whether true tolerance to the tree nut in question was achieved.

We studied 906 tree nut and peanut challenges in 680 consecutive children and teenagers, ages 4 month to 19 years, referred for assessment of suspected nut allergy. Based on our data, the traditional 3-mm wheal cutoff for a negative SPT was associated with a high rate of false-positive and false-negative results. The diagnostic accuracy of SPT increased when higher cutoff wheal diameters were used. We identified the SPT wheal diameters that predicted a positive food challenge with >95% accuracy (cashew, hazel nut, walnut, and sesame: ≥8 mm). We could not confidently determine the 95% positive predictive value (PPV) for almond, pistachio, pecan, and brazil nut. For pecan (≥7 mm) and brazil nut (≥8 mm), the PPV remained below 95%, despite a high specificity and high positive test likelihood ratio. This may be a result of a relatively small sample size for some of the tree nuts. These findings are summarized in Table I.

Using these predictive SPT decision points, the need for a formal oral food challenges to make a definitive diagnosis in our cohort was reduced by 33% (peanut), 56% (tree nuts), and 53% (sesame), respectively (data not shown). Monitoring for possible development of tolerance by repeated SPT may enable clinicians to assess resolution of tree nut allergy over years. SPT offers advantages in terms of cost and the turnover time of results. It is important to emphasize that the SPT wheal diameter correlates with the likelihood of a positive nut challenge but not with the clinical severity of adverse reactions.8 SPT should be