

## Letter to the Editor

## Anaphylaxis to apple and orange seed

## To the Editor:

Childhood fruit allergy is relatively common, with up to 3% of 3-year-olds having allergy to citrus fruit,<sup>1</sup> the best-studied example being oranges.<sup>2</sup> Susceptible subjects generally present with symptoms of oral allergy syndrome (also known as pollen-food syndrome) with associated pollen sensitization.<sup>3</sup> Although there are a limited number of reports of patients reacting to citrus seeds in the absence of clinical reactivity to fruit pulp/peel,<sup>4,5</sup> there are no previous reports of apple seed allergy.

We have recently managed 3 children with anaphylactic reactions to fruit seeds, all of whom could tolerate the fruit pulp. A 6-year-old girl experienced a generalized nonanaphylactic reaction to an unknown constituent of a fruit salad and had a positive skin prick test (SPT) response to orange seed (9.5 mm). SPT responses were also positive to fresh mango (5 mm), kiwi fruit (9 mm), and lemon seed (10 mm) but negative to orange pulp. At a formal in-hospital open food challenge (OFC), she had anaphylaxis (abdominal pain, urticaria, and shortness of breath with oxygen desaturation) after ingestion of a single orange seed.

The second child, a 5-year-old girl, had anaphylaxis after ingestion of a cut slice of orange but had a negative SPT response to orange pulp and tolerated a full seedless orange at a subsequent OFC. The SPT response was positive to fresh orange seed (15 mm) and mandarin and grapefruit seeds, and she was therefore given a diagnosis of citrus seed allergy.

Both children had coexisting peanut allergy (diagnosed on the basis of a previous clinical reaction and confirmatory positive SPT response/specific IgE measurement). Interestingly, they were also sensitized on SPTs to cashew and pistachio, a finding consistent with the few cases of citrus seed allergy previously reported in the literature.<sup>4,6</sup>

The third child was a 15-month-old boy with previous anaphylaxis to kiwi fruit and a history of perioral erythema after exposure to banana and strawberry. He presented with anaphylaxis on first exposure to commercially produced apple and oatmeal baby food (containing apple puree, apple juice, oats, and cinnamon extract). Within minutes of ingesting 2 teaspoons, he vomited, became lethargic, and had cyanosis with drooling, requiring multiple (3) doses of intramuscular adrenaline. He was subsequently noted to have facial angioedema and widespread urticaria by the attending medical staff. SPT responses were positive to the ingested baby food (5 mm), apple seed (4 mm), and orange seed (4 mm) and negative to fresh apple, cinnamon, and oats. He also had positive SPT responses to kiwi, strawberry, peanut, cashew, pistachio, and sesame. He had previously eaten and tolerated apple and oats and was able to tolerate homemade apple puree, cinnamon, and oats at a subsequent in-hospital OFC. The manufacturer confirmed that the baby food implicated is produced in a factory that does not handle other potential allergens, including nuts and other fruit products. We are informed that a manufacturer's analysis of the batch did not demonstrate evidence of contamination, although these data and the method of analysis were not made available to us. However, the manufacturer did confirm that apples, typically of the species *Malus domestica* × *Malus sylvestris* (commonly known as Granny Smith), are not routinely cored during production. We therefore

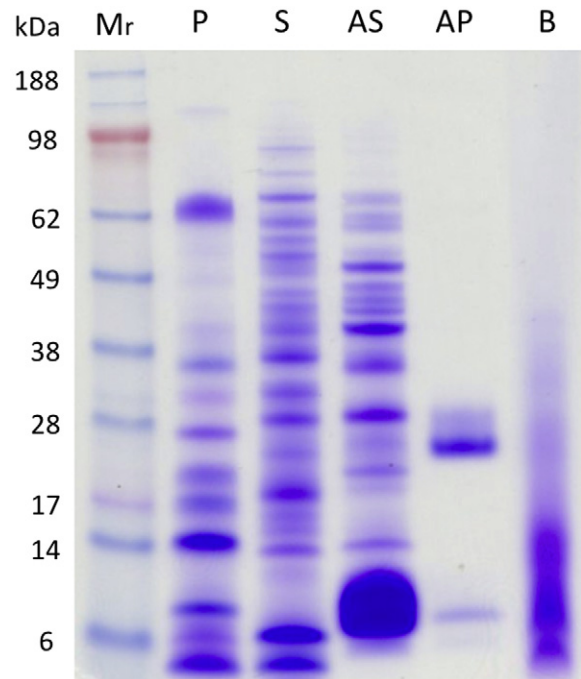


**FIG 1.** Analysis of apple and other protein extracts. Peanut (P), sesame seed (S), apple seed (AS), apple pulp (AP), and apple-containing baby food (B) extracts were resolved under reducing conditions with 4% to 12% SDS-PAGE and stained with Coomassie brilliant blue. Mr, Molecular mass markers.

hypothesize that the commercially produced puree contained apple seeds, which might have been crushed during production.

To further characterize the nature of the allergy in this third patient, we prepared extracts of peel/pulp and seeds from Granny Smith apples, peanut, and sesame seed, as previously described.<sup>7</sup> We also attempted extraction of the apple and oat baby food. Analysis of these extracts by means of SDS-PAGE is shown in Fig 1. Protein bands were visible between 9 and 95 kDa for the apple seed extract, with strong bands at 9, 28, 36, 40, and 49 kDa. Unfortunately, it was not possible to obtain a clean extraction from the commercial baby food. The patient's serum IgE bound to proteins from the apple seed extract, with particularly strong binding at 49 and approximately 70 kDa (Fig 2). Binding was also observed to the known allergens peanut and sesame but not to the apple pulp, which is consistent with the SPT results. No IgE binding to the extracts was observed with the nonatopic control serum (data not shown). We speculate that the apple seed proteins on immunoblotting represent novel allergens because they do not correspond to characterized allergens of apple, sesame, or peanut.

To our knowledge, this is the first report of allergy to (noncitrus) apple seed, and interestingly, the child was also sensitized on SPTs to sesame, orange, and lemon seeds, raising the possibility of cross-sensitization to multiple seeds. The 3 children on whom we report had all previously tolerated the fruits in question, and we postulate that it was only when the inner seed was exposed through cutting or crushing that a reaction occurred, as previously suggested by Zhu et al.<sup>5</sup> Testing for fruit allergy generally uses

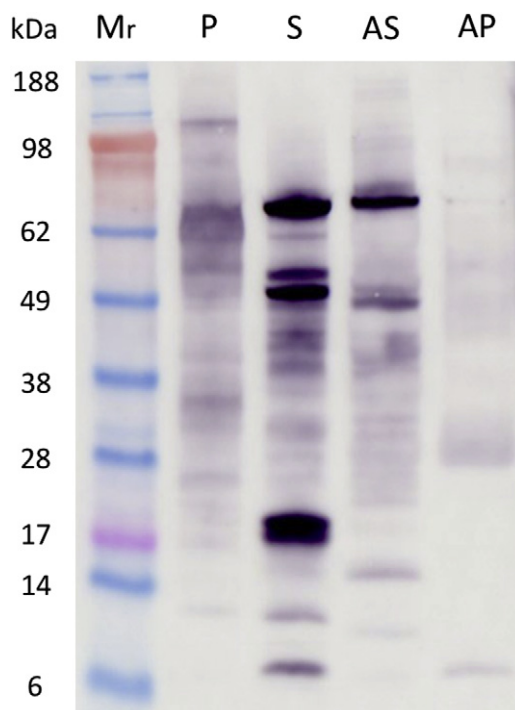


**FIG 2.** IgE immunoblotting of peanut (P), sesame seed (S), apple seed (AS), and apple pulp (AP) extracts. Extracts were resolved with 4% to 12% SDS-PAGE under reducing conditions and then transferred to nitrocellulose and probed with the patient's serum at a 1:5 dilution. *Mr*, Molecular mass markers.

extracts from the pulp rather than the seed, and therefore the clinician might be falsely reassured about the safety of fruits in a patient allergic to fruit seeds.

We suggest that allergy to fruit seeds is far more common than currently appreciated but is probably underrecognized. Clinicians might not consider the role of seeds during the workup for presumed fruit allergy, and confusion might arise if symptoms only develop if the seed is cut or crushed. It is therefore important

to consider fruit seeds as a potential cause of fruit-associated allergic reactions in which the precipitating allergen is not known. Our data, together with those previously reported, suggest a possible association between allergy to fruit seeds and nuts, particularly to peanut, cashew, and pistachio. We therefore recommend considering fruit seeds to be a potential cause of apparent idiopathic anaphylaxis in patients with nut allergies.

*Paul J. Turner, FRACP, PhD<sup>a,b</sup>*

*Paul E. A. Gray, FRACP<sup>a</sup>*

*Melanie Wong, FRACP, PhD<sup>a</sup>*

*Nirupama Varese, MSc<sup>c</sup>*

*Jennifer M. Rolland, PhD<sup>c</sup>*

*Robyn O'Hehir, FRACP, PhD<sup>c</sup>*

*Dianne E. Campbell, FRACP, PhD<sup>a,b</sup>*

From <sup>a</sup>the Department of Allergy and Immunology, Children's Hospital at Westmead, Sydney, Australia; <sup>b</sup>the Discipline of Pediatrics and Child Health, School of Medicine, University of Sydney, Sydney, Australia; and <sup>c</sup>the Department of Immunology, Monash University, Melbourne, Australia. E-mail: [paulyt@doctors.net.uk](mailto:paulyt@doctors.net.uk).

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