

Not so sweet: True chocolate and cocoa allergy



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Clinical Implications

- We report a case series of oral food challenge—confirmed, IgE-mediated chocolate/cocoa allergy. Given the usual assumption that reactions to chocolate and cocoa are due to cross-reactivity with other allergens, this report should raise awareness for chocolate and cocoa as allergens.

TO THE EDITOR:

Food allergy to chocolate and cocoa is considered possible, but there has been no report to date of challenge-proven, IgE-mediated allergy to chocolate or cocoa. Although population studies cite a prevalence of self-reported chocolate/cocoa allergy of 0.5% to 0.7% in select populations,¹ self-reported food allergy is notoriously inaccurate, and objective testing was not used to corroborate chocolate or cocoa allergy status in these studies.¹ Most empirically defined chocolate and cocoa allergies are thought to be due to cross-contamination from common allergens, including peanut,² tree nuts, or milk.^{3,4} Here, we report for the first time a case series of oral food challenge (OFC)-confirmed, IgE-mediated chocolate/cocoa allergy.

Patient 1 presented at age 2 years with a history of atopic dermatitis, reactive airway disease, rhinoconjunctivitis triggered by dog exposure, and report of several reactions encompassing hives and vomiting to cow's milk-based formula and yogurt. She had also experienced symptoms on 2 occasions when eating chocolate, which were attributed to the presence of milk in the chocolate. Her cocoa skin prick test (SPT) result and serum allergen-specific immunoglobulin E (sIgE) levels are shown in Figure 1, A. She outgrew her milk allergy and was fully tolerating milk and dairy foods by age 5 years, at which time allergy testing was repeated and cocoa OFC was offered given the unclear history. At age 7 years, she returned for a physician-supervised OFC to cocoa, using cocoa-based chocolate chips (Enjoy Life) and chocolate chip minis (Made Good Chocolate Chip Granola Minis), both manufactured in an allergy-conscious facility without peanut or tree nuts, and with strict cross-contamination precautions such that individuals with milk, peanut, and/or tree nut allergies can safely consume these products. Her OFC, described in Figure 2, A, was positive, with vomiting, wheezing, respiratory distress, and generalized hives. She was treated with intramuscular epinephrine and oral antihistamines.

Patient 2 presented at age 8 years with a history of wheezing in the past year after eating a pecan cookie dipped in chocolate, and additional report of itchy ears after eating ice cream with chocolate. Her cocoa SPT result and sIgE levels are shown in Figure 1, B, and she was also found to be sensitized to tree nuts. She was scheduled the following year for a physician-supervised

OFC to cocoa, using cocoa unsweetened powder (Hershey's) mixed with previously tolerated raspberry yogurt. Cocoa is the only ingredient in this product, and it is manufactured in an allergy-conscious facility with cross-contact precautions. Her challenge, described in Figure 2, B, was positive, with abdominal pain, coughing, and wheezing. She was treated with intramuscular epinephrine and oral cetirizine.

Patient 3 had multiple food allergies, asthma, allergic rhinitis, and atopic dermatitis. He presented for a follow-up visit at age 18 years, while avoiding peanut, tree nuts, chickpea, lentil, green pea, and chocolate (cocoa SPT result and sIgE levels in Figure 1, C). He had had a prior physician-supervised OFC to chocolate at age 7 years where after ingesting a square of chocolate (Hershey's), he developed generalized hives, cough, and wheezing that was treated with intramuscular epinephrine. Because his cocoa sIgE level had decreased to less than 0.35 kU_A/L at age 18 years, he was scheduled for a repeat OFC to cocoa using Hershey's milk chocolate bar. This product is made in a peanut-free plant with cross-contact precautions on a dedicated line that does not manufacture tree nut items. His challenge (Figure 2, C) was again positive, with facial swelling, facial flushing, generalized hives, and wheezing. He was treated with 2 doses of intramuscular epinephrine, albuterol, cetirizine, and prednisolone.

Cocoa beans are extracted from the cocoa fruit pod of cacao trees (*Theobroma cacao*).⁵ Cacao trees belong to the *Malvaceae* family, which also includes species from which cotton, okra, and durian fruit are harvested.⁵ Cocoa beans yield chocolate via a process involving fermentation, roasting, and grinding.⁵ Cocoa powder, a mix of carbohydrates, fat, and protein, is produced by removing part of the cocoa butter from that processed product.

As a source of vitamins, minerals, and polyphenols, cocoa has been considered as a nutraceutical.⁶ Studies of ovalbumin-sensitized rats have suggested that a cocoa-enriched diet over 4 weeks is associated with lower antiovalbumin IgE synthesis and decreased total serum IgE concentration.⁷ In lymph node cells, TNF- α and IL-10, but not IL-4, production was reduced in rats on cocoa-enriched diet versus controls.⁷ The investigators attributed the above immunomodulatory effects to flavonoids contained in cocoa. Although this previous work suggests potential benefits to cocoa ingestion, the cases we have described here demonstrate that like many other food proteins, cocoa also has the potential to be allergenic on its own.

Although challenge-proven IgE-mediated allergy to chocolate/cocoa has not been previously reported, there have been reports of allergic symptoms in individuals sensitized to chocolate/cocoa via occupational exposure. Specifically, chocolate confectionery workers show a high level of cocoa sensitization (31% of a group of 71 confectionery workers), and there is increased prevalence of asthma and dyspnea in sensitized versus nonsensitized workers.⁸ No chocolate or cocoa allergen has yet been characterized. What is known is that a 2S cocoa seed albumin storage polypeptide has high sequence similarity (>52%) and identity (>38%) to several plant 2S albumins known to be allergenic, including those in Brazil nut.⁹ The presence of theobromine and caffeine in chocolate may also be responsible for pseudoallergic symptoms that can be reported as allergic symptoms.

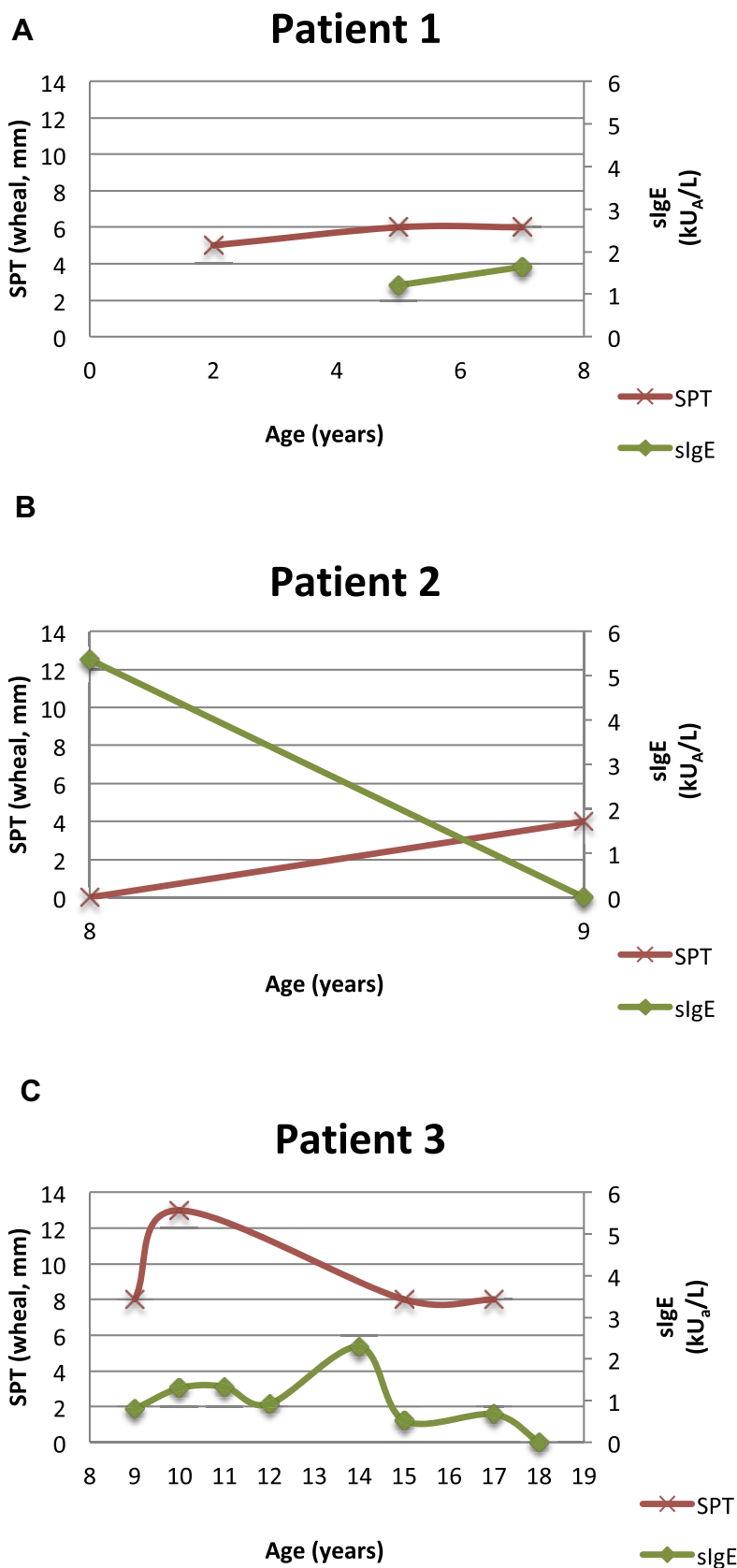


FIGURE 1. Cocoa SPT wheal and serum sIgE levels over time for **A**, patient 1; **B**, patient 2; and **C**, patient 3. SPTs were performed with cocoa allergen extract, histamine control, and saline control from Stallergenes Greer (Boston, Mass) and supplies from Roehling Medical Lancaster, LLC (Denver, Pa). All subjects responded appropriately to histamine and saline controls. SPT wheal diameters were measured with a ruler 15 minutes after placement. Serum sIgE levels were measured using Thermo Fisher ImmunoCAP (Waltham, Mass).

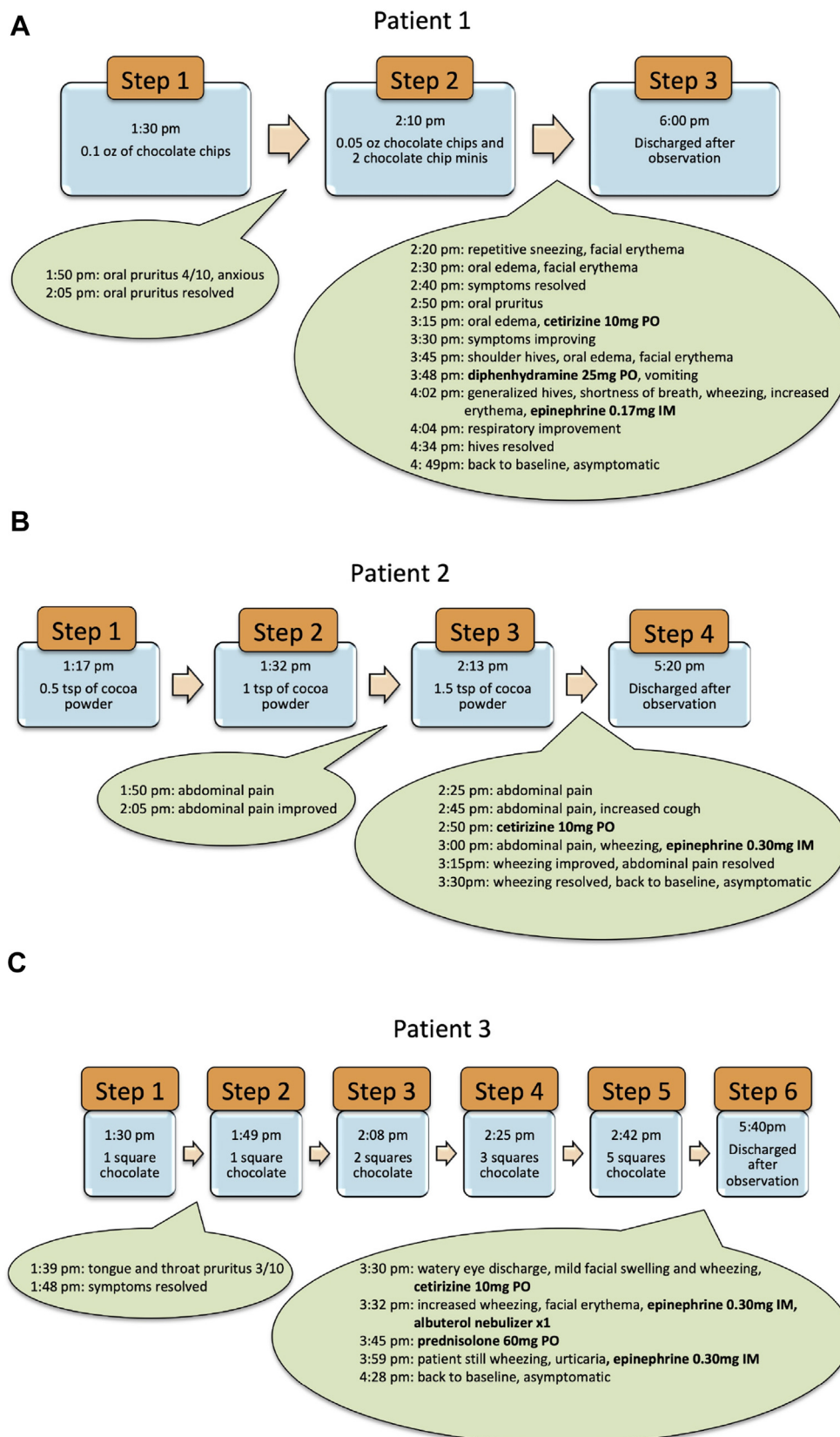


FIGURE 2. Detailed descriptions of chocolate/cocoa OFCs for (A) patient 1, (B) patient 2, and (C) patient 3. *IM*, Intramuscular; *PO*, per os (by mouth); *tsp*, teaspoon.

In summary, we have presented a case series of challenge-proven, IgE-mediated chocolate/cocoa allergy where all 3 patients reacted convincingly with anaphylaxis to allergist-supervised chocolate/cocoa OFCs. Reported chocolate and cocoa allergies are commonly attributed to cross-reactivity with other allergens that often accompany chocolate and cocoa, such as peanut, tree nuts, and milk, but our report shows that true allergy to chocolate and cocoa is possible.

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