

Exercise-induced anaphylaxis after food contaminant ingestion in double-blinded, placebo-controlled, food-exercise challenge

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The current incidence of food-dependent, exercise-induced anaphylaxis (FDEIA) is unknown. There is no specific diagnostic test, triggers are numerous, and non-immunologic anaphylaxis can occur after postprandial exercise. An exercise-induced anaphylaxis (EIA) link to a food contaminant is also lacking, and open-challenge studies¹ have recommended a food-exercise challenge in the workup for suspected FDEIA. We describe a patient with EIA triggered by food colonized by *Penicillium lanoso-caeruleum* and diagnosed with FDEIA by means of double-blind, placebo-controlled, food-exercise challenge (DBPCFEC).

CASE HISTORY

A 14-year-old boy with asthma since age 10 years had three episodes of EIA from May 1995. The patient had a history of hypersensitivity to grass, mites, and several fungi. Flushes, pruritus, urticaria, and cough occurred after a school running event that took place 2 hours after the patient ate a meal of salami (with its casing), pasta, Parmesan cheese, tomatoes, beef, bread, and an apple. These symptoms were treated with 200 µg of salbutamol administered through a metered-dose inhaler. Two months later, the patient experienced colic, urticaria, flushes, periorbital and labial edema, cough, and hypotension after a running event that took place 3 hours after a meal of rice, bread, butter, Parmesan and mascarpone, spinach, carrots, and a peach. He did not respond to 400 µg of salbutamol, and the school doctor administered antihistamines and a betamethasone injection. Four days later while playing soccer, the patient experienced pruritus, flushes, periorbital and labial edema, cough, and dyspnea followed by asthma and loss of consciousness 3 hours after a meal of pasta, Parmesan, bread, beef, artichokes, potatoes, red wine, a peach, and a pear. These symptoms were treated with epinephrine, chlorpheniramine, and hydrocortisone injections before he was admitted to our unit 6 hours later.

METHODS

Basal function tests showed slight obstruction, but postchallenge FEV₁ and forced expiratory flow at 25% to 75% of forced vital capacity did not indicate exercise-induced asthma. Total

Abbreviations used

DBPCFEC:	Double-blind placebo-controlled food-exercise challenge
EIA:	Exercise-induced anaphylaxis
FDEIA:	Food-dependent, exercise-induced anaphylaxis

serum IgE levels were 187 IU/ml. During the diagnostic workup, the patient was advised to avoid food 6 to 8 hours before training, to discontinue any sport at the first onset of symptoms, to carry readily injectable epinephrine with him, and to exercise only in the presence of a companion trained to administer the epinephrine if needed.²

Cultured salami casings from the patient's home yielded *P. lanoso-caeruleum* colonies, which were suspended in glycerol 50% at 1:10 vol/vol for use in skin prick tests and food challenges. One month later, skin prick tests were done with molds, wheat, rice, peanut, tomato, carrot, apple, peach, cow's milk, cow's milk casein, beef, and pork extracts (all supplied by Lofarma). Skin prick tests (> 3 mm diameter, positive) showed a positive reaction for molds, with the strongest positive (≥ 5 cm Ø) reaction associated with *P. lanoso-caeruleum*.

To exclude FDEIA caused by foods, a food-exercise, treadmill, ergonomic stress test¹ was carried out 120 minutes after challenge with pasta, mascarpone, Parmesan, beef, artichoke, and apple. No symptoms developed.

Challenges with *P. lanoso-caeruleum* were administered on separate days. First, a double-blind, placebo-controlled food challenge was planned with four doubling doses (0.5, 1, 2, and 4 ml) of *P. lanoso-caeruleum* suspension delivered at 30-minute intervals, with the excipient as placebo.³ Because the results of the double-blind, placebo-controlled food challenge were negative up to 4 ml (160 mg of mold), eight successive DBPCFECs were carried out. The third DBPCFEC was suspended after 5 minutes because pruritus, urticaria, lip edema, cough, and bronchospasm developed. Arterial blood pressure of 85/50 mm Hg (115/75 mm Hg pretest), a 39.5% fall in FEV₁ and a 61.3% fall in forced expiratory flow at 25% to 75% of forced expiratory flow rate were recorded, and epinephrine and hydrocortisone injections were administered. The symptoms remitted within a few minutes. The blinding code was broken, and it was found that the meal contained 1 ml of mold suspension (40 mg of mold).

DISCUSSION

Although molds and mites contaminating foods are known to cause contact urticaria⁴ and food allergy,⁵ this

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is the first report of a food and exercise-induced reaction to any type of contaminant. Neither ingestion of *P. lanoso-caeruleum* nor running was sufficient to trigger the reaction. There was also an association between FDEIA and exercise-induced bronchospasm, which often accompanies childhood asthma. This is also the first time that DBPCFEC has been used to confirm a diagnosis of FDEIA. There are recent reports of anaphylaxis confirmed by food-exercise challenge,¹ but they rely on open procedures. The blinding of challenges, despite the difficulties introduced by undetermined history, multiple suspected foods, problems with masking foods, and finding suitable placebos is now accepted as all important to food allergy research.³ Diagnostic error can also induce unnecessary dietary modifications, and fasting before athletic performance² and the unpredictability of onset of this disease may deter patients from participating in sports. We could prescribe realistic prophylactic measures once the trigger was established. At 1-year

follow-up the patient is still healthy and has been able to take part in track events with no relapse of FDEIA reported.

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Evaluation of an in vitro assay for fire ant venom-specific IgE

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The safety and efficacy of venom for diagnosis (by skin testing and in vitro testing) and therapy of allergy to winged hymenopterans are clearly established. However, fire ant whole-body extract (WBE) remains the only reagent commercially available for testing and immunotherapy. We have previously evaluated performance (relative to venom skin testing) of a venom RAST, venom ELISA, and a WBE solid phase for the Pharmacia CAP system (PCS).^{1,2} The WBE solid phase had performance characteristics similar to those of venom RAST and venom ELISA. This study was designed to evaluate the laboratory performance of a prototype fire ant venom extract solid phase for the PCS by comparing its performance with that of fire ant WBE solid phase and titrated venom intradermal skin testing.

Abbreviations used

ASM:	Alternate Scoring Method
PCS:	Pharmacia CAP System
ST:	Skin test
WBE:	Whole-body extract

METHODS

Thirty-two subjects were recruited from a fire ant endemic area in the Southeastern United States. Nineteen of the subjects were patients clinically evaluated because of a history of systemic reaction after a fire ant sting. Thirteen of the subjects had not had a systemic reaction after a fire ant sting and served as control subjects. The study was conducted under a protocol approved by the Human Assurance Committee, and informed consent was obtained from all subjects. All subjects received titrated intradermal skin testing with a fire ant venom preparation available for research use (Vespa Laboratories Inc., Spring Mills, Pa.). Blood was drawn, and the serum was frozen at -70°C until analysis. The prototype venom, the commercially available whole-body solid phases, and other reagents were kindly provided by the manufacturer (Pharmacia & Upjohn, Uppsala, Sweden). The assays were performed in duplicate by the standard quantitative PCS method with the manufacturer's

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