

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.

We thank Gabriel R. Bouygue for his critical assistance in the preparation of the manuscript.

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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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J Allergy Clin Immunol 1997;100:425-7.

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0091-6749/97 \$5.00 + 0 1/54/82998

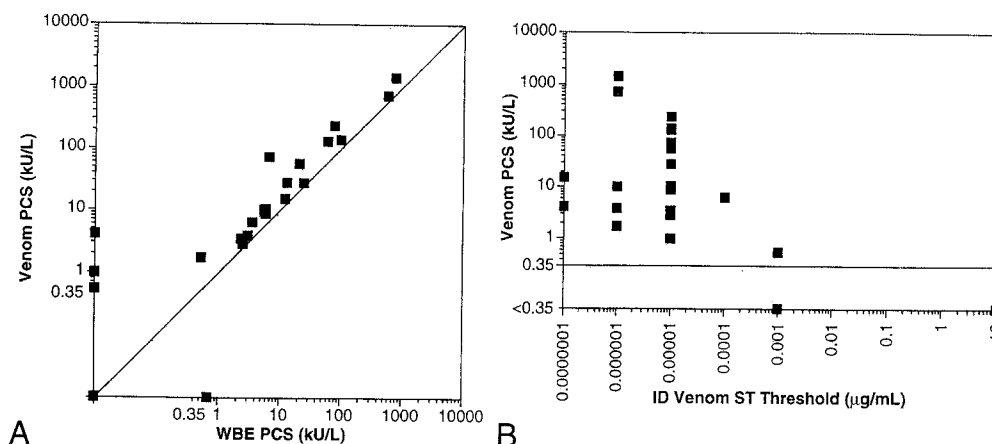


FIG. 1. Correlation of WBE and venom PCS assays (A); correlation of quantitative intradermal venom skin testing with venom PCS (B).

TABLE 1. Sensitivity and specificity of WBE and venom PCS assays relative to venom skin testing

Method	No. of positive venom ST results	No. of negative venom ST results	Sensitivity	Specificity
WBE PCS (>0.35 kU/L)	18/22	1/10	0.82	0.90
WBE PCS (ASM-positive)	18/22	1/10	0.82	0.90
Venom PCS (>0.35 kU/L)	21/22	0/10	0.95	1.00
Venom PCS (ASM-positive)	22/22	0/10	1.00	1.00

recommended 0.35 kU/L cutoff. This method provides results in the range of 0.35 to 100 kU/L on the basis of a total IgE reference curve calibrated to the World Health Organization standard for IgE. Additionally, results were calculated by using the manufacturer's alternate scoring method (ASM), which reports nonquantitative results. In this method any sample producing a response greater than or equal to 60% of the response produced by the 0.35 kU/L total IgE calibrator was considered positive. Venom RAST and venom ELISA had been performed in previously reported studies.^{1,2}

RESULTS

Results of WBE and venom assays correlated well (Spearman $\rho = 0.94$, Fig. 1). Venom PCS assay results also correlated well with venom RAST (Spearman $\rho = 0.90$) and ELISA results (Spearman $\rho = 0.87$). Quantitative intradermal venom skin test (ST) results also correlated with results of the venom assay (Spearman $\rho = -0.76$, Fig. 1). For a given level of ST reactivity, a wide range of specific IgE levels was observed.

Of the 32 subjects, 22 had positive ST results (at a concentration of 1 μg/ml or less) and 10 had negative ST

results. Of the subjects with positive ST results, 19 of 22 had a prior systemic reaction, 2 of 22 had a large local reaction only, and 1 of 22 had no systemic or large local reaction. Of the 10 subjects with negative ST results, six reported a previous fire ant sting but had not had a systemic or large local reaction. Four had no history of a fire ant sting. The venom solid phase had both higher sensitivity and specificity than the WBE solid phase when compared with venom skin testing. The manufacturer's 0.35 kU/L quantitative cutoff resulted in a sensitivity of 0.95 and a specificity of 1.00, whereas use of the manufacturer's lower ASM cutoff resulted in a sensitivity of 1.00 without a loss of specificity.

One serum sample from a control subject with a negative ST response was positive by WBE assay but negative by venom assay. This patient had also reacted to WBE (Hollister-Stier, Spokane, Wash.) by titrated intradermal skin test at 1:100 wt/vol. One control subject with no history of a systemic or large local reaction had positive results with both WBE and venom skin testing at 1:10,000,000 wt/vol. The WBE assay was negative by standard and ASM scoring, and the venom assay was positive at 4.04 kUa/L (class 3).

DISCUSSION

In this patient population, in vitro results from the venom solid phase were qualitatively similar to those of the venom intradermal ST, particularly when the manufacturer's less conservative ASM³ was used. Fire ant venom RAST and ELISA correlated well, and both correlated well with quantitative intradermal skin testing. The venom solid phase appears to be more sensitive and specific than the WBE solid phase. These results underscore the importance of using fire ant venom for diagnostic testing.

Reagents, including the prototype solid phase, were kindly provided by Pharmacia & Upjohn, Uppsala, Sweden.

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Upper gastrointestinal obstruction associated with Claritin-D 24 Hour Extended Release tablets

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The licensing application for Claritin-D 24 Hour Extended Release tablets (Claritin-D 24 Hour) was approved by the Food and Drug Administration on August 23, 1996, for the treatment of antihistamine-responsive symptoms and congestion associated with seasonal allergic rhinitis. Each Claritin-D 24 Hour tablet contains 10 mg of loratadine in the tablet film coating for immediate release and 240 mg of pseudoephedrine sulfate in the core, which is released slowly, allowing for once-daily administration. Although the Claritin-D 24 Hour tablet is large (Fig. 1), there were no patient-reported problems with swallowing the pill or complaints of the tablet becoming lodged in the throat or esophagus in the clinical trials conducted in support of the safety and efficacy of the drug product. Shortly after approval, five reports of throat or esophageal obstruction were received by the Division of Pharmacovigilance and Epidemiology at the Food and Drug Administration. These case reports are summarized and discussed below.

CASE REPORTS

Patient 1

A 19-year-old woman with a history of asthma reported that the first dose of Claritin-D 24 Hour tablets became lodged in her throat. Paramedics were called, and the Heimlich maneuver was performed without success. After transport to a local emergency facility, she was seen by an ear, nose, and throat physician who sprayed her throat with a local anesthetic in preparation for direct laryngoscopy. The introduction of the instrument caused her to cough up the tablet, presumably as a result of induction of her gag reflex. The patient recovered without sequelae. Her medical history was unremarkable for upper gastrointestinal disease, and she had no history of difficulty swallowing tablets.

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J Allergy Clin Immunol 1997;100:427-8.
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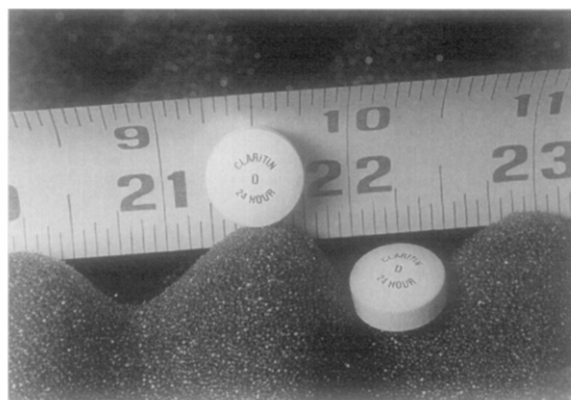


FIG. 1. Claritin-D 24 Hour Extended Release tablet (scale in inches).

Patient 2

A 37-year-old woman reported that the first dose of Claritin-D 24 Hour tablets became lodged in her throat and she was unable to swallow the tablet despite the fact that the tablet had been taken with a full 8-ounce glass of water. She was taken to the local emergency department, and an "esophageal sphincter obstruction" was diagnosed. Esophagoscopy was performed while the patient was under general anesthesia, and the tablet was removed from the cricopharyngeal area. The examining physician reported no anatomic deformity and believed that the "tablet size and coating caused an esophageal sphincter spasm." The patient recovered without sequelae.

Patient 3

A 67-year-old woman reported that the first dose of Claritin-D 24 Hour tablets became lodged in her throat, and she required transfer to a local emergency department. A barium swallow revealed complete esophageal obstruction requiring esophagoscopy while the patient was under general anesthesia. The tablet was removed, and the patient recovered without sequelae. A second direct visualization ruled out anatomic stricture. She had similar problems with large vitamin tablets in the past; however, she had never previously required mechanical removal of these tablets.