Safety and efficacy of fire ant venom in the diagnosis of fire ant allergy

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Thirty-three adult patients who had had systemic allergic reactions to fire ant stings and 33 insect-nonallergic control subjects were skin tested with single lots of Solenopsis invicta (Sol i) *fire ant venom (IFAV) and two commercially available imported fire ant whole body extracts (IFA WBEs). All three extracts were analyzed for protein concentration.* Sol i *II and* Sol i *III concentrations were each assayed by means of two ELISAs with complementary monoclonal antibodies, one species specific and one cross-reactive. Radioallergosorbent test (RAST) to IFAV and both IFA WBEs was performed on sera from all study subjects. Both IFA WBEs contained high concentrations of fire ant body proteins.* Sol i *II and III concentrations each varied twofold between the two IFA WBE preparations. Patients were generally more reactive to IFAV than IFA WBE by skin testing and RAST. IFAV RAST appeared to be a more sensitive assay than IFA WBE RAST. No adverse reactions occurred to skin testing with IFAV, but intradermal testing with higher concentrations of IFA WBE caused delayed large local reactions in 16 of 30 (53%) control subjects. These reactions were attributed to the large amounts of extraneous body proteins in IFA WBE. These results (1) demonstrate that skin testing with IFAV is safe, (2) indicate that IFAV is more potent than IFA WBE, and (3) suggest that IFAV may be the superior reagent for diagnosis of fire ant allergy. (J ALLERGY CLIN IMMUNOL 1992;90:653-61.)*

Key words: Solenopsis invicta, *venom, whole body extract, diagnosis, fire ant allergy*

In contrast to experience with apidae and vespidae, the role of venom in diagnosis and treatment of fire ant allergy has not been clearly established.[1-4] Studies have confirmed that imported fire ant whole body extracts (IFA WBE) contain clinically relevant allergens that are apparently effective for diagnosis and treatment of fire ant allergy.[5-13] However, variability of skin test reactivity and treatment failures with IFA WBEs have been reported.[7, 11, 14, 15] Crossed immunoelectrophoresis (CIE) and RAST-inhibition studies of commercial WBE preparations have revealed qualitative and quantitative differences in antigen composition and allergenic potency.[6, 16, 17] The differences in skin test reactivity among various IFA WBE preparations have been attributed to variability in allergenic venom protein content.[5-7, 9, 17-19]

Abbreviations used

CIE:	Crossed immunoelectrophoresis
ELISA:	Enzyme-linked immunosorbent assay
IFAV:	Imported fire ant venom
IFA WBE:	Imported fire ant whole body extract
IND:	Investigational new drug
RAST:	Radioallergosorbent test
Sol i:	*Solenopsis invicta*
wt/vol:	Weight/volume
vol/vol:	Volume/volume

This is the report of an investigational new drug (IND) study of the safety and effectiveness of commercially produced fire ant venom (IFAV) in the diagnosis of fire ant allergy. In vitro testing has shown the composition and antigenicity of this prototype fire ant venom product to be comparable to pure, hand-milked IFAV.[5, 20-22] This is the first report of diagnostic skin testing with this IFAV product.

The objectives of this study were to (1) evaluate safety and (2) assess the effectiveness of IFAV compared with IFA WBE in the diagnosis of fire ant allergy.

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TABLE I. Results of diagnostic tests in allergic patients

Patient no.	IFA skin test			IFA RAST		
	WBE no. 1 (wt/vol)	WBE no. 2 (wt/vol)	IFAV (dilution)	WBE no. 1	WBE no. 2 (% binding)	IFA
1	1×10^{-6}	1×10^{-6}	1×10^{-6}	2.5	2.6	26.1
2	1×10^{-6}	1×10^{-6}	1×10^{-5}	1.8	2.2	24.2
3	1×10^{-5}	1×10^{-5}	1×10^{-4}	2.2	2.7	10.3
4	1×10^{-5}	1×10^{-5}	1×10^{-3}	0.2	0.4	0.8
5	1×10^{-6}	1×10^{-6}	1×10^{-4}	3.6	3.8	33.9
6	1×10^{-6}	1×10^{-6}	1×10^{-5}	0.3	0.5	2.1
7	1×10^{-6}	1×10^{-6}	1×10^{-4}	1.2	1.2	8.6
8	1×10^{-5}	1×10^{-5}	1×10^{-4}	1.3	1.2	15.6
9	1×10^{-5}	1×10^{-5}	1×10^{-5}	0.2	0.5	5.0
10	1×10^{-6}	1×10^{-6}	1×10^{-5}	0.8	0.2	6.4
11	1×10^{-5}	1×10^{-5}	1×10^{-4}	0.4	0	3.0
12	1×10^{-6}	1×10^{-4}	1×10^{-4}	0.8	1.9	2.4
13	1×10^{-6}	1×10^{-6}	1×10^{-5}	1.7	2.0	10.0
14	1×10^{-6}	1×10^{-6}	1×10^{-6}	7.3	3.7	22.1
15	1×10^{-6}	1×10^{-6}	1×10^{-6}	2.1	2.5	9.9
16	1×10^{-6}	1×10^{-5}	1×10^{-5}	1.0	.7	21.8
17	1×10^{-6}	1×10^{-6}	1×10^{-5}	2.6	3.2	14.8
18	1×10^{-6}	1×10^{-6}	1×10^{-5}	0.3	0.7	2.4
19	1×10^{-6}	1×10^{-6}	1×10^{-6}	0.7	0.7	0.6
20	1×10^{-7}	1×10^{-7}	1×10^{-6}	1.3	0.3	12.5
21	1×10^{-6}	1×10^{-6}	1×10^{-5}	2.5	3.0	19.0
22	1×10^{-6}	1×10^{-6}	1×10^{-4}	3.0	2.4	11.6
23	1×10^{-6}	1×10^{-6}	1×10^{-5}	8.0	6.7	17.3
24	1×10^{-5}	1×10^{-6}	1×10^{-6}	.8	0.6	10.7
25	1×10^{-6}	1×10^{-6}	1×10^{-6}	8.5	6.8	30.3
26	1×10^{-6}	1×10^{-6}	1×10^{-6}	0.4	0.4	3.7
27	1×10^{-7}	1×10^{-7}	1×10^{-7}	1.4	1.3	12.8
28	1×10^{-6}	1×10^{-6}	1×10^{-5}	5.8	3.7	19.9
29	1×10^{-6}	1×10^{-6}	1×10^{-5}	2.6	1.5	11.5
30	1×10^{-6}	1×10^{-6}	1×10^{-5}	1.0	0.8	6.5
31	1×10^{-6}	1×10^{-6}	1×10^{-6}	4.9	3.2	16.3
32	1×10^{-5}	1×10^{-5}	1×10^{-5}	2.4	1.9	17.4
33	1×10^{-7}	1×10^{-7}	1×10^{-7}	0.6	1.2	5.7

MATERIAL AND METHODS

Study subjects

Sixty-six subjects were enrolled in the study under conditions of informed consent as approved by the Medical College of Georgia Institutional Review Board. The patient group consisted of 33 patients with a history of a systemic reaction to a fire ant sting within the past year and no history of other Hymenoptera allergy. The control group consisted of 33 normal subjects living in a fire ant endemic area, but with no history of insect allergy.

Antigen preparations

Glycerinated *Solenopsis invicta (Sol i)* venom, lot no. 9005/906252 was obtained from Vespa Laboratories, Spring Mills, Pa. Freshly prepared, glycerinated *Sol i* WBEs were purchased from Greer Laboratories, Lenoir, N.C. (lot no. GB7-13B-1A7) and Hollister-Stier Laboratories, Spokane, Wash. (lot no. H10E8081).

Skin testing

All patients and control subjects were skin tested with IFAV and both IFA WBE preparations. After screening prick skin tests with 1×10^{-6} dilutions, intradermal skin tests were performed with 0.02 to 0.03 ml of 1×10^{-6} dilutions and tenfold increments in concentration until a positive skin test was elicited. Skin tests were considered positive if a wheal at least 6×6 mm and erythema at least 11×11 mm developed within 15 minutes and the wheal was at least 3 mm greater than the negative control. Control subjects were also tested with serial tenfold dilutions of the 50% glycerinated diluent used in the IFAV and IFA WBE preparations.

TABLE II. Results of diagnostic tests in control subjects

Control no.	IFA skin tests			IFA RAST		
	WBE no. 1 (wt/vol)	WBE no. 2 (wt/vol)	IFAV (dilution)	WBE no. 1	WBE no. 2 (% binding)	IFAV
1	1×10^{-4}	1×10^{-3}	0	0.2	0.0	0.0
2	1×10^{-3}	1×10^{-3}	0	0.3	0.0	0.0
3	1×10^{-2}	1×10^{-2}	0	0.2	0.0	0.4
4	1×10^{-4}	1×10^{-4}	1×10^{-4}	0.1	0.5	0.2
5	1×10^{-4}	1×10^{-4}	1×10^{-3}	0.3	0.0	4.0
6	1×10^{-3}	1×10^{-3}	1×10^{-2}	0.8	0.3	0.9
7	2×10^{-1}	1×10^{-1}	0	0.1	0.0	0.5
8	1×10^{-2}	1×10^{-2}	1×10^{-1}	0.1	0.3	0.8
9	1×10^{-3}	1×10^{-3}	0	0.1	0.3	0.0
10	1×10^{-2}	1×10^{-2}	0	0.0	0.0	0.0
11	2×10^{-1}	1×10^{-1}	1	0.0	0.2	1.0
12	1×10^{-2}	1×10^{-2}	0	0.2	0.0	0.3
13	1×10^{-4}	1×10^{-4}	1×10^{-3}	0.6	1.1	3.0
14	1×10^{-2}	1×10^{-1}	0	0.0	0.3	0.3
15	1×10^{-3}	1×10^{-3}	1×10^{-1}	1.3	1.3	2.9
16	2×10^{-1}	1×10^{-1}	0	0.0	0.0	0.2
17	1×10^{-3}	1×10^{-3}	1×10^{-2}	0.3	0.0	1.3
18	2×10^{-1}	1×10^{-1}	0	0.2	0.3	0.3
19	1×10^{-4}	1×10^{-3}	1×10^{-3}	0.3	0.0	0.5
20	1×10^{-3}	1×10^{-3}	1×10^{-2}	0.0	0.1	0.4
21	1×10^{-2}	1×10^{-2}	0	0.3	0.4	0.5
22	1×10^{-2}	1×10^{-2}	1	0.0	0.9	0.3
23	0	0	0	0.2	0.9	0.9
24	2×10^{-1}	1×10^{-1}	0	0.0	0.4	0.2
25	2×10^{-1}	1×10^{-1}	1	0.1	0.4	0.2
26	1×10^{-4}	1×10^{-3}	1×10^{-3}	0.3	0.0	0.5
27	1×10^{-2}	1×10^{-1}	0	0.2	0.5	0.6
28	2×10^{-1}	1×10^{-1}	1	0.0	0.0	0.0
29	1×10^{-6}	1×10^{-6}	1	3.5	1.1	0.5
30	2×10^{-1}	1×10^{-1}	1×10^{-1}	0.2	1.3	0.2
31	0	1×10^{-1}	0	0.0	0.0	0.0
32	1×10^{-4}	1×10^{-4}	1×10^{-2}	0.2	0.0	0.4
33	2×10^{-1}	1×10^{-1}	1×10^{-1}	0.0	0.5	0.0

RAST assays

Approximately 10 ml of serum was obtained from each study subject and stored at −20° C until used for RAST analysis. RAST was performed by a standard method previously described for IFAV and WBEs.[23]

Protein analysis

Total protein concentration of each fire ant skin test reagent was determined by the Pierce dye-binding assay as previously described.[24]

Sol i and *Sol i* III assays

Each fire ant skin test reagent was assayed for content of *Sol i* II and *Sol i* III content. Species specific and species cross-reactive monoclonal antibodies were prepared against *Sol i* II and *Sol i* III. A double-antibody ELISA was performed with use of biotin-streptavidin as previously described.[5, 26, 27] One antibody was used to coat the plate and capture antigen. The second antibody was biotinylated and was used for detection.

Statistical analysis

Sensitivity, specificity, and predictive value of a positive test was calculated for each of the study methods (Table III). Results of skin testing with IFAV and IFA WBE were compared on the basis of protein concentrations of 0.01 μg/ml or less and 0.1 μg/ml or less as well as *Sol i* II and *Sol i* III concentrations of 0.01 μg/ml or less. Sensitivity, specificity, and predictive value of a positive test was calculated for the RAST procedures based on an optimal cutoff binding value of 2.0% for IFA venom and 0.7% for both IFA WBE preparations. The RAST cutoff value for IFAV

TABLE III. Results of fire ant allergen tests with 95% confidence limits*

Fire ant allergen tests	Sensitivity	Specificity	Predictive value of positive test
IFA venom skin test (protein ≤ 0.01 μg/ml)	97% (84.2% - 99.9%)	97% (84.2% - 99.9%)	97% (84.7% - 99.9%)
IFA WBE skin test (protein ≤ 0.01 μg/ml)	76% (57.7% - 88.9%)	97% (84.2% - 99.9%)	96% (80.4% - 99.9%)
IFA venom skin test (protein ≤ 0.1 μg/ml)	100% (91.7% - 100%)	88% (71.8% - 96.6%)	87% (71.9% - 95.6%)
IFA WBE skin test (protein ≤ 0.1 μg/ml)	97% (84.2% - 99.9%)	97% (84.2% - 99.9%)	97% (84.7% - 99.9%)
IFA venom skin test (*Sol i* II 0.01 μg/ml)	97% (84.2% - 99.9%)	97% (84.2% - 99.9%)	97% (84.7% - 99.9%)
IFA WBE skin test (*Sol i* II 0.01 μg/ml)	97% (84.2% - 99.9%)	97% (84.2% - 99.9%)	97% (84.7% - 99.9%)
IFA venom skin test (*Sol i* III 0.01 μg/ml)	97% (84.2% - 99.9%)	97% (84.2% - 99.9%)	97% (84.7% - 99.9%)
IFA WBE skin test (*Sol i* III 0.01 μg/ml)	100% (91.7% - 100%)	97% (84.2% - 99.9%)	97% (84.7% - 99.9%)
IFA venom RAST (+ ≥2%)	94% (79.8% - 99.3%)	82% (64.5% - 93.0%)	84% (68.0% - 93.8%)
IFA WBE no. 1 RAST (+ ≥ 0.07%)	85% (68.1% - 94.9%)	91% (75.7% - 98.1%)	90% (74.3% - 98.0%)
IFA WBE no. 2 RAST (+ ≥0.7%)	82% (64.5% - 93.0%)	82% (64.5% - 93.0%)	82% (64.5% - 93.0%)

*95% confidence limits expressed as percents (%) in parentheses.

is higher than normally used and was chosen to maximize the separation between allergic and control subjects. The value of 0.7% specific binding used for the IFA WBE preparations was chosen by the same method. It is twice the negative control value obtained for each of the WBEs with a series of venom nonreactive sera.

Estimates of 95% confidence limits were calculated on the basis of the F-distribution.[28]

RESULTS

Demographics

The two study groups were closely matched demographically. The mean age of the patient group was 33 years, with a range of 22 to 56 years. The mean age of the control group was 34 years, with a range of 22 to 54 years. Both study groups had a similar male to female ratio of approximately 2:1.

Patients reported an average of 7.6 fire ant stings responsible for inducing systemic reactions. The number of stings per episode ranged from 1 to 45. Although 30% reported a single fire ant sting, 55% suffered three or more stings.

All control subjects were tested while living in a fire ant endemic area; however, 12 of 33 (36%) denied ever having been stung by fire ants. Of the 21 controls who reported previous stings, 10 subjects had been stung by fire ants within the past year.

Antigenic protein

The concentration of total protein was 635 μg/ml in IFA WBE no. 1 at 1:10 wt/vol concentration and 280 μg/ml in IFA WBE no. 2 at 1:20 wt/vol concentration. The protein content of the IFAV was 40 μg/ml. The difference in protein concentration between IFAV and IFA WBE preparations is attributed to the relatively large amounts of extraneous body proteins in the IFA WBE preparations.

The two IFA WBE preparations differed in *Sol i* II and *Sol i* III concentrations. IFA WBE no. 1 contained

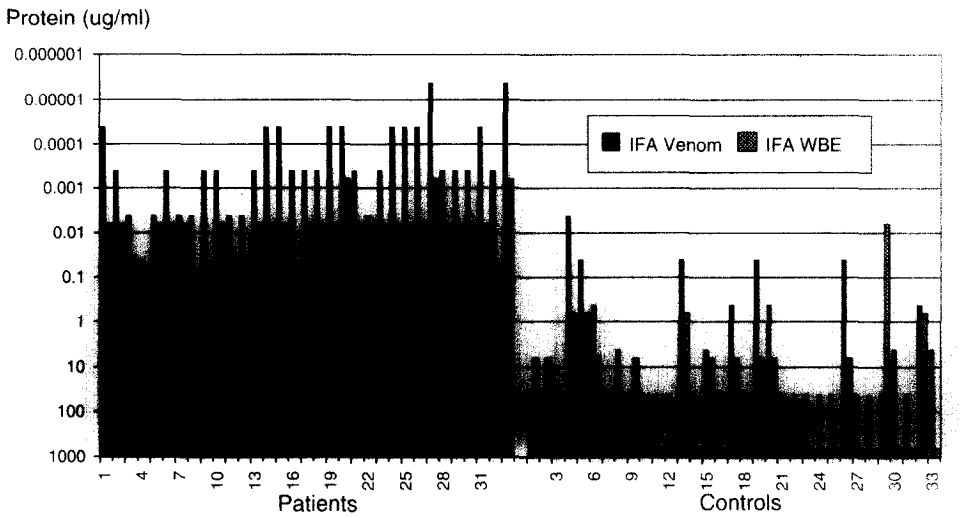

FIG. 1. Bar graph illustrates skin test reactivity of patients and control subjects to IFA venom and IFA WBE on the basis of protein concentration (μg/ml) shown on the abscissa of $\log_{10}$ scale. Responses of control subjects nonreactive to all IFA antigen concentrations are indicated by the highest concentration available for testing.

14 μg/ml of *Sol i* II at 1:10 wt/vol concentration whereas the IFA WBE no. 2 contained 7 μg/ml at 1:20 wt/vol concentration. IFA WBE extract no. 1 contained 14 μg/ml of *Sol i* III, whereas IFA WBE no. 2 contained 16 μg/ml. IFA venom contained 24 μg/ml of *Sol i* II and 18.5 μg/ml of *Sol i* III. The protein concentration of all antigens used in the study were determined by the Pierce-dye binding assay, which underestimates *Sol i* II relative to amino acid analysis because of its low content of aromatic amino acids.

Skin test results

Fire ant skin test reactivity in patients and control subjects to IFAV and IFA WBE on the basis of protein concentration is illustrated in Fig. 1. Patients allergic to fire ants generally reacted to protein concentrations in IFAV approximately tenfold lower than in IFA WBE, demonstrating that IFAV is approximately 10 times more potent than IFA WBE on the basis of protein content. Skin test reactivity was similar for both IFA WBE preparations despite a twofold difference in *Sol i* III content. Patients reacted to lower concentrations of all antigen preparations than did control subjects. However, the controls reacted to concentrations slightly lower than anticipated on the basis of results of previous studies.[6, 7, 9] This may be related to increased potency of the freshly prepared allergenic extracts used in this study.

At least 21 of 33 (64%) control subjects living in a fire ant endemic area reported having been previously stung by fire ants. Skin tests were completely nonreactive to IFAV, even at maximal concentration, in 15 of 33 (45%) of control subjects. This finding contrasts with IFA WBE skin testing that was completely nonreactive in only a single control subject (3%).

Differences in reactivity to IFAV and IFA WBE based on content of *Sol i* antigens was less striking (Figs. 2 and 3). No significant differences were observed in skin test reactivity between IFAV and IFA WBE based on *Sol i* II and *Sol i* III concentrations.

Adverse effects

Skin testing with IFAV caused no adverse reactions in patients or control subjects even at the highest concentration used for testing. However, skin testing with both IFA WBE preparations at concentrations ranging from 2.8 μg/ml to 635 μg/ml caused large delayed local reactions in 16 of 30 (53%) control subjects. Skin testing with the glycerinated diluent produced no irritant reactions at concentrations lower than 5%.

RAST results

Allergic patients showed greater serum RAST reactivity to IFAV than IFA WBE as demonstrated by significantly higher percent binding (Fig. 4). Control subjects demonstrated low levels of RAST reactivity (percent binding) to both IFA antigens. The differences in IFAV RAST reactivity between patients and controls was greater than that for IFA WBE.

DISCUSSION

Skin testing with IFAV appears to be a safe diagnostic procedure. No adverse reactions were produced by IFAV in either patients or control subjects. This contrasts with our experience with IFA WBE, which caused large delayed local reactions in 16 of 30 (53%)

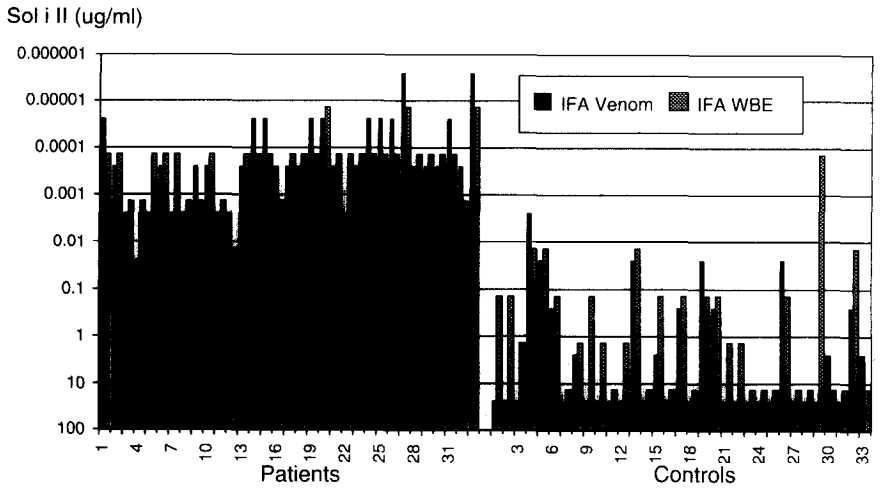

FIG. 2. Bar graph illustrates skin test reactivity of patients and control subjects on the basis of *Sol i* II concentration (μg/ml) on $\log_{10}$ scale.

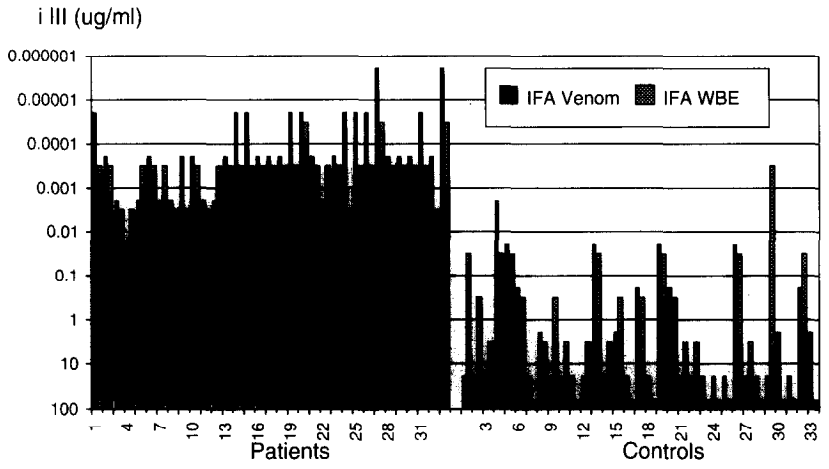

FIG. 3. Bar graph illustrates skin test reactivity of patients and control subjects on the basis of *Sol i* III concentration (μg/ml) on $\log_{10}$ scale.

control subjects at higher extract concentration ranging from 2.8 μg/ml to 635 μg/ml. Both IFA WBE preparations caused similar large local reactions that usually peaked in size and severity at approximately 24 hours and persisted for up to 3 weeks. These reactions appear to be clinically distinct from the late-phase IFA sting reactions reported by deShazo et al.[29] It is unlikely that these reactions were due to glycerine, since delayed reactions did not occur to equivalent amounts of glycerine in IFAV. Furthermore, similar delayed reactions were not reproduced by skin testing with glycerine alone. These reactions were considered most likely to be due to extraneous body proteins contained in IFA WBE. A number of the fire ant body proteins are potentially immunogenic but do not appear to cause clinically significant allergic sting reactions.[5, 6, 16, 25] It is conceivable that such reactions could possibly contribute to morbidity associated with skin testing and potentially interfere with the ability to achieve adequate protective allergen doses during the course of immunotherapy with IFA WBE.

IFA WBE skin test titers among the control group in this study were slightly higher than anticipated. There are at least two possible explanations for this observation. Freshly prepared lots of glycerinated IFA WBEs were purchased for use in this study. One IFA WBE preparation actually had a higher *Sol i* III concentration than IFAV. Second, our control subjects were recruited from a fire ant endemic population; 21 of 33 (64%) had previously sustained fire ant stings, and 10 reported having been stung within the past year. Fire ant skin test reactivity in control subjects who confirm or deny having been stung by fire ants is illustrated in Fig. 5.

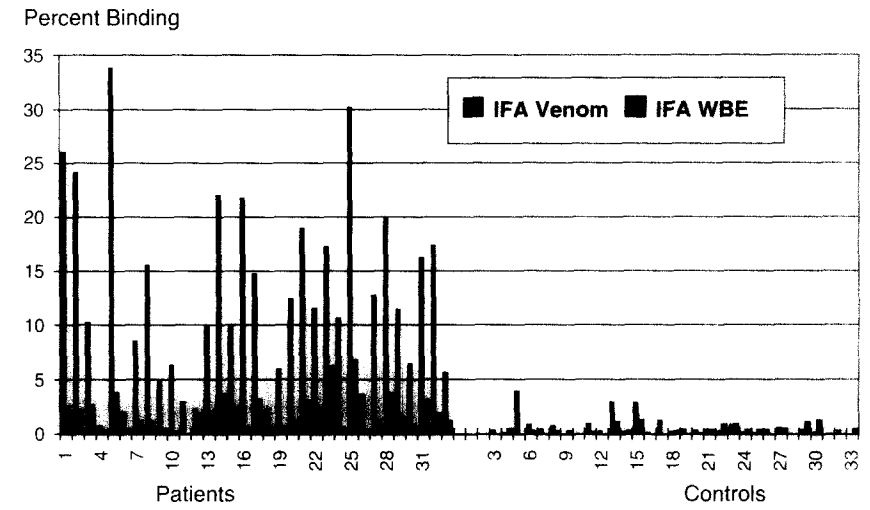

FIG. 4. Bar graph illustrates serum RAST reactivity of patients and control subjects to IFA venom and IFA WBE shown as percent binding.

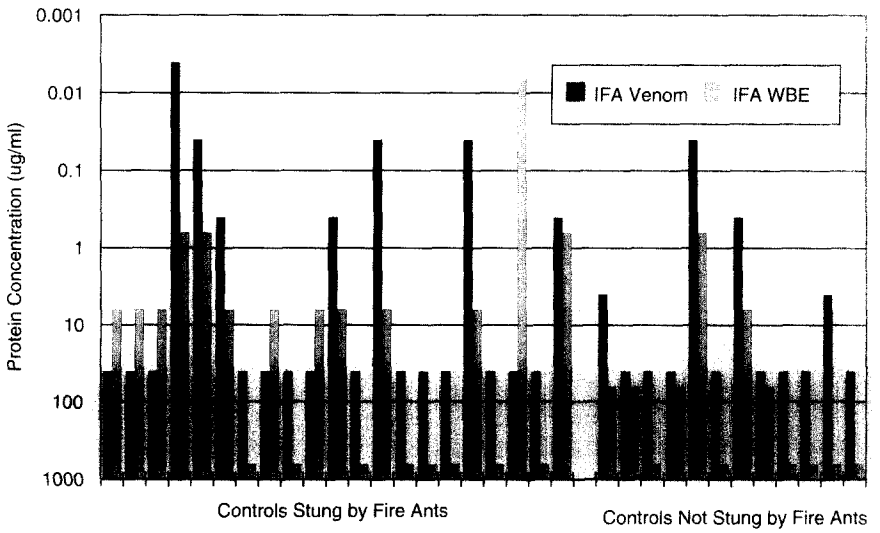

FIG. 5. Bar graph illustrates skin test reactivity to IFA venom and IFA WBE in control subjects who have and have not been stung by fire ants.

Although the skin test titers were slightly higher than anticipated, the frequency of positive reactivity to IFA WBE in the control population was not unanticipated. Increased fire ant skin test reactivity among control subjects living in an endemic area has been previously reported.[9, 26] The incidence of skin test reactivity to IFA WBE has been reported to be as high as 23% in allergic patients with no history of insect sting allergy who live in fire ant endemic areas.[30] Similar asymptomatic sensitization has also been demonstrated for other Hymenoptera venoms as well as inhalant allergens.[31-33]

Skin test reactivity to IFAV and IFA WBE has previously been compared on the basis of wt/vol or vol/vol concentrations.[6-9] The present study was designed to compare reactivity to IFA allergens on the basis of protein, *Sol i* II, and *Sol i* III allergen concentrations at which a positive skin test is elicited.

On the basis of protein concentration, IFA venom appears to be approximately tenfold more potent than IFA WBE. In general, allergic patients reacted to approximately tenfold lower protein concentrations of IFAV than IFA WBE. Reactivity to IFAV and IFA WBEs were nearly equivalent when the concentrations of *Sol i* II and *Sol i* III allergens were used as the basis for comparison. A possible explanation for these divergent results may be the dilution of clinically relevant IFA allergens by relatively large amounts of extraneous IFA whole body proteins.

Fire ant venom appears to be a more sensitive skin

test reagent than IFA WBE at a protein concentration of 0.01 μg/ml or less. However, IFA WBE appears to be equally sensitive at a protein concentration of 0.1 μg/ml or less. The specificities of the antigen preparations used for skin testing did not appear to differ significantly. In addition, there was no difference in sensitivity or specificity between IFA venom and either WBE at *Sol i* II or *Sol i* III concentrations of 0.01 μg/ml or greater.

Patients with fire ant allergy were also found to be more reactive to IFAV than to IFA WBE as determined by RAST. This finding is consistent with results of previous studies that have shown IFAV RAST to be more sensitive than WBE RAST.[8, 9, 17] However, although IFAV RAST has a higher sensitivity, it has a lower specificity than IFA WBE no. 1 RAST at the selected cutoff values for percent binding. The lower specificity leads to a lower predictive value of a positive test; thus IFA WBE no. 1 RAST, although less sensitive, is more specific.

A difference appears to exist in specificity between the two IFA WBE preparations with use of $+\leq 0.7\%$ for the RAST, leading to a 90% versus 82% predictive value of positive test for the two preparations. The two WBEs used in this study also differed significantly in *Sol i* II and *Sol i* III content. These findings are consistent with previous reports of antigenic variability among fire ant IFA WBE preparations.[6, 19]

However, despite the difference in *Sol i* II and *Sol i* III concentrations, the two IFA WBEs produced similar skin test reactivity. The twofold difference is not so readily apparent on the $\log_{10}$ scale used in the study.

In summary, the results of this study suggest that IFAV may be superior to IFA WBE as a diagnostic reagent on the basis of the following findings:

1. IFAV is approximately 10 times more potent on the basis of protein content;
2. IFAV RAST is more sensitive than IFA WBE RAST;
3. Skin testing with IFAV appeas to be more sensitive than with IFA WBE at a protein concentration of 0.01 μg/ml;
4. IFA WBE contains irrelevant body proteins;
5. Higher concentrations of IFA WBE cause large delayed local reactions;
6. IFAV is associated with better test subject comfort, tolerance, and acceptance.

In conclusion, these findings suggest that IFAV is the more potent, more sensitive, and better tolerated skin test reagent for diagnosis of fire ant allergy.

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The relationship between late asthmatic responses and antigen-specific immunoglobulin

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The aim of this study was to examine the relationships between allergen-induced early and late airway responses and antigen-specific IgE, IgG, and lymphocyte subsets in blood and bronchoalveolar lavage (BAL). Brown Norway rats were sensitized at 7 weeks of age with ovalbumin (1 mg s.c.) with use of Bordetella pertussis *as an adjuvant. Three weeks after sensitization, animals were anesthetized and challenged with an aerosol of ovalbumin (5% wt/vol in saline) for 5 minutes. Each animal was studied for 8 hours with repeated measurements of lung resistance. Blood was obtained at 0, 1, 2, and 3 weeks before ovalbumin challenge. Ovalbumin-specific IgE and IgG were determined by ELISA. No specific antibody was detectable before sensitization. Ovalbumin-specific IgE and IgG rose between 1 to 2 weeks after sensitization and peaked at 3 weeks. The IgE level did not correlate with the magnitude of either the early or the late responses. In a similar manner no correlation existed between the magnitude of specific IgG and the late response. However, a significant inverse correlation ($r = -0.73$; $p < 0.01$) occurred between specific IgG and the early response. No correlation occurred between the ratio of helper (W3/25+) to suppressor (OX-8+) lymphocytes in blood and BAL and airway responses to allergen. The size of the early and late responses were correlated, suggesting a common stimulus. Despite the blunting of the early response by repeated sensitization the late response was unaffected, suggesting that the factors that determine the physiologic expression of the early and late responses are different. (J ALLERGY CLIN IMMUNOL 1992;90:661-9.)*

Key words: *BN rats, lymphocyte subsets, allergic bronchoconstriction*

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