

Comparison of Venom and Whole-Body Rast and Intradermal Testing in Vespid-Sensitive Patients¹

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Abstract. 14 patients clinically hypersensitive to vespid sting by history, 6 patients with large local reactions and 10 control subjects were skin tested with serial two- and tenfold dilutions of venom and whole-body extract of yellow jacket, wasp, and white-faced hornet antigens. Radioallergosorbent test determinations with the same antigens were also made. Determination of minimal reactive dose by skin testing distinguished control and hypersensitive patients groups for all three antigens using either venom or whole body extract. Yellow jacket venom skin testing detected 12 of 14 patients considered clinically hypersensitive. This was not the case with the other two venoms, possibly because most of the patients were yellow jacket sensitive, or any of the whole-body extracts. The Radioallergo-sorbent test was less useful than venom skin testing in detecting patients considered clinically sensitive.

Introduction

Since the introduction of whole-body extract (WBE) in 1930 [1] for diagnosis and treatment of Hymenoptera sting hypersensitivity, there has been controversy over the efficacy of this material. This disagreement has been sharpened by the lack of good correlation between histories and the results obtained from skin testing. Consequently, decisions regarding treatment have rested primarily on the history. Recently, *Valentine et al.* [2] reported that 30% of patients

who suffered apparent IgE-mediated systemic reactions after Hymenoptera stings failed to react adversely following a subsequent sting under controlled conditions in hospital. These stings by insects to which the patients were history and skin test positive, were administered without previous immunotherapy or medical pretreatment. This study showed the difficulty of evaluating results of immunotherapy with either WBE or venom without prior confirmation of immunologic hypersensitivity. The 98% success rate [3] of treatment reported with WBE may include a number of false-positive results, perhaps as many as 40% [2]. It

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is possible, however, that there is some efficacy. In a retrospective study, the *Insect Allergy Committee of the American Academy of Allergy* [4] reported that 26% of untreated patients stung a second time experienced a more severe reaction compared to 4.6% treated with WBE. Because these data are retrospective and uncontrolled, they do not constitute 'hard' evidence for therapeutic efficacy.

In an attempt to overcome this problem, investigators have searched for decades to find more accurate methods to establish the presence of Hymenoptera sensitivity including testing with pure venom [5–7], *in vitro* histamine release [8, 9], and the radioallergosorbent test (RAST). *Reisman et al.* [10] have advocated the venom RAST as an accurate technique for detecting stinging insect hypersensitivity. It is generally felt that the RAST is less sensitive although more specific than the intradermal test [11, 12]. We undertook the present study to compare the diagnostic accuracy of venom and whole-body RAST and intradermal testing

in vespid-sensitive patients selected by history alone.

Materials and Methods

Patients

20 patients were referred to the Allergy Clinic of the Roosevelt Hospital, New York, for diagnostic testing. A history questionnaire was completed during the initial interview and 14 patients were classified as clinically hypersensitive since they experienced one or more of the following symptoms within 60 min after a single Hymenoptera sting: (1) generalized urticaria; (2) angioedema; (3) generalized erythema; (4) asthma; (5) generalized pruritus; (6) laryngeal edema, or (7) cardiovascular collapse. In addition, there had to have been at least a 4-week interval since the adverse reaction and no previous treatment or testing for at least 3 months. Table I presents the age and sex distribution of the subjects. None had any chronic or acute medical illnesses. All patients read the study protocol and signed an informed consent. 6 patients were classified as having had only excessively large local reactions after the sting; 2 of these had symptoms that might have represented a systemic reaction but did not meet the above criteria.

10 subjects without a history of atopy or an

Table I. Historical data

	Subjects			Age, years		Interval sting to testing		Interval treatment to testing	
	n	males	females	mean	range	mean	range	mean	range
Systemic reactions ¹	14	8	6	37	21–55	3.1 years	2 months to 11 years	7.2 years ²	5 months to 18 years
Excessive local reactions	6	1	5	39	26–58	10 months	2 months to 3 years	1 of 6 was treated 1 year prior to testing	
Controls	10	4	6	32	25–43	7 stung	childhood to 1 year prior to testing	No treatment	

¹ One or more of the following symptoms: generalized urticaria, angioedema, generalized erythema, generalized pruritus, asthma.

² 7 of 14 received immunotherapy.

adverse reaction to Hymenoptera stings served as controls. 7 of these remembered having been stung without incident in the past years.

Antigens

WBE of wasp, yellow jacket (YJ) and hornet were obtained from Center Laboratories, Port Washington, N. Y. All extracts were standardized in protein nitrogen units (PNU) for comparison of end points (EP). Dried venoms of wasp (Polistes; Pol), YJ and white face hornet (WFH) were obtained from Dr. Allen Benton, State College, Pa. Venom sacs were dissected from the insect, cleaned, washed and put in a tissue homogenizer for about 1 sec to break the sac walls. The venom was then centrifuged, put through a Millipore filter and lyophilized. Very little sac protein was found in the lyophilized product. Protein content of the venom was determined by the Lowry method. The venom was weighed and diluted to a concentration of 500 $\mu\text{g/ml}$ (including approximately 30% alanine buffer). Skin test EP figures were subsequently corrected for buffer content. The diluent for skin testing was Evans buffered saline containing 0.03% human serum albumin kindly supplied by the Community Blood Council of Greater New York, Inc. as a stabilizer. Each venom antigen was filtered through a Swinnex-25 Millipore filter and tested for sterility. Fresh solutions of 500 $\mu\text{g/ml}$ were made weekly and diluted in tenfold and twofold series before testing. No dilution used was more than 8 days old.

Studies in vitro

Before skin testing, serum was obtained for measurement of allergen-specific antibody to each of the wasp, YJ or hornet venoms and whole-body antigens by the RAST. The RAST analysis was performed as described by Ceska *et al.* [13]. Concentrations of 1 mg vespid venom in 2 cm^2 bicarbonate diluent or 0.15 ml of 1:10 w/v WBE were utilized for 10 discs. Each serum was run in duplicate. A known positive serum to all three vespids was included in each run (patient Me.). Control sera were run with each assay. The same lots of venom were used for skin testing and RAST. A coefficient of variation for the RAST assay was determined using the same positive serum in five separate runs and was found to be 14%. RAST values were expressed as percent of the total cpm bound (tables Va, b). A 'clinically positive' RAST was determined according to reference units ob-

tained from Pharmacia Laboratories, Piscataway, N.J., consisting of filter paper discs fixed with birch pollen allergen and incubated with dilutions of pooled serum from patients highly allergic to birch pollen. The dilutions were assigned arbitrary units proportional to the concentration of reference serum (50 being five times more concentrated than 10). Cpm were plotted on a log-log graph against these units. Under these conditions the curve between 2 and 10 U is a straight line and can be used to read results in RAST units for undiluted or diluted sera. Results were expressed in these units. A level of 2 or more units was considered to be significant.

Studies in vivo

Skin testing was performed by the intradermal technique using a 0.25- cm^3 B-D Yale precision glass syringe fitted with a 3/8-in No. 26 g disposable needle. Testing was started with 0.2 PNU/ml for wasp WBE, 0.4 PNU/ml for both hornet WBE and YJ WBE, and 0.003 $\mu\text{g/ml}$ of each venom. The test volume of 0.01 ml was accurately injected; all skin testing was performed and read by the same investigator (T.N.). Testing was done serially using twofold stronger mixtures (0.01 ml) until an EP was obtained, or until 500 $\mu\text{g/ml}$ of venom or 20,000–40,000 PNU/ml of WBE were reached without an EP. The EP was read as that strength at which a patient's reading changes from 1+ to 2+. (Testing was continued until a 3+ confirmatory reaction was obtained.) If the change from 1+ to 2+ occurred between two consecutive testing strengths, the concentration eliciting that change was extrapolated. In some subjects the EP was not quite reached with the highest concentration used. In these cases EP figures appear slightly higher than the top concentration tested as a result of extrapolation (table IIa, b). 1+ corresponds to a 3- to 5-mm wheal with surrounding erythema and no pseudopods, 2+ to a 5- to 10-mm wheal with surrounding erythema and no pseudopods, and 3+ to a 10-mm or to a greater wheal with pseudopods and surrounding erythema. Data were reported in minimal reactive doses (MRD), i.e., the concentration used multiplied by the volume injected (0.01 cm^3).

Statistical Analysis

Student's *t* test was used to evaluate differences of MRD among the various patient groups. Since one cannot directly compare PNU and micrograms,

Table IIa. Mean reactive doses of two- and tenfold venom skin testing

Patients	Venom, μg						RAST
	twofold dilution			tenfold dilution			
	YJ	Pol	WFH	YJ	Pol	WFH	
<i>Systemic reactions</i>							
1 Co. ¹	0.25	0.67	0.11	0.04	0.34	0.04	neg.
2 Bs.	0.08	0.34	0.45	0.16	0.35	1.6	+ YJ
3 Ph. ¹	0.007	0.005	0.003	0.01	0.003	0.0004	+ YJ
4 Gr. ¹	0.06	5.38	0.90	0.04	3.58	0.36	+ YJ
5 Eo. ¹	0.002	0.02	0.06	0.00004	0.004	0.004	neg.
6 Ba.	0.45	0.90	1.79	0.36	3.58	0.36	neg.
7 Me.	0.002	0.11	0.009	0.02	0.11	0.15	+ YJ, Pol, WFH
8 Bi. ¹	0.0004	0.004	0.005	0.0002	0.004	0.0002	+ YJ
9 Gi.	0.003	0.01	0.009	0.02	0.004	0.004	+ YJ
10 Hag.	0.14	4.03	0.56	0.22	2.02	2.02	+ YJ
11 Bu. ¹	0.11	3.58	0.67	0.04	3.58	1.96	neg.
12 Ly.	3.58	3.58	3.58	3.58	3.58	3.58	neg.
13 Hat. ¹	0.007	1.79	0.45	0.02	0.36	0.03	neg.
14 Pe.	0.003	5.38	0.06	0.02	3.58	0.35	neg.
Mean $\pm$ SD	0.33 $\pm$ 0.94	1.84 $\pm$ 2.09	0.61 $\pm$ 0.98	0.32 $\pm$ 0.94	1.50 $\pm$ 1.68	0.74 $\pm$ 1.10	
<i>Large local reactions</i>							
15 Ap.	0.11	0.34	0.90	0.04	0.36	1.97	neg.
16 Ag.	0.90	0.0004	0.04	3.58	0.0003	0.04	neg.
17 Su. ¹	0.17	2.69	0.96	0.08	1.97	0.04	neg.
18 Ho.	0.06	3.58	5.38	0.20	1.97	1.97	neg.
19 Za.	3.58	3.14	3.14	3.58	1.96	0.35	neg.
20 Wi.	0.90	2.24	0.34	0.36	1.16	0.11	neg.
Mean $\pm$ SD	0.95 $\pm$ 1.34	1.95 $\pm$ 1.65	1.79 $\pm$ 2.06	1.30 $\pm$ 1.76	1.23 $\pm$ 0.88	0.74 $\pm$ 0.95	
<i>Controls</i>							
1 Wa.	ND	ND	ND	3.58	1.93	3.58	neg.
2 Az.	ND	ND	ND	3.58	3.58	0.35	neg.
3 Na.	ND	ND	ND	3.58	3.58	3.58	neg.
4 Fo.	ND	ND	ND	1.96	5.38	1.96	neg.
5 Se.	ND.	ND	ND	0.36	1.93	0.19	neg.
6 Fa.	ND	ND	ND	1.97	3.58	1.97	neg.
7 On.	ND	ND	ND	3.58	3.58	3.58	neg.
8 La.	ND	ND	ND	1.93	3.58	3.58	neg.
9 Go.	ND	ND	ND	1.89	3.58	3.58	neg.
10 Ne.	ND	ND	ND	1.93	1.93	0.36	neg.
Mean $\pm$ SD				2.43 $\pm$ 1.09	3.26 $\pm$ 1.57	2.27 $\pm$ 1.50	

ND = Not determined.

¹ Had previously received immunotherapy.

Table IIb. Mean reactive doses of two- and tenfold WBE skin testing

Patients	Whole-body extract, PNU						RAST
	twofold dilution			tenfold dilution			
	YJ	Pol	WFH	YJ	Pol	WFH	
<i>Systemic reactions</i>							
1 Co. ¹	7.0	25.3	20	8.4	4.0	6.0	neg.
2 Bs.	2.2	6.8	0.3	1.4	2.8	0.23	neg.
3 Ph. ¹	0.88	0.30	0.06	0.42	0.38	0.12	neg.
4 Gr. ¹	7.0	19.0	60.0	8.4	27.1	6.0	neg.
5 Eo. ¹	0.32	0.01	3.7	0.84	0.009	6.0	neg.
6 Ba.	140	1.43	100	42	4.6	30	neg.
7 Me.	0.05	0.06	3.2	0.42	1.9	0.6	neg.
8 Bi. ¹	0.08	1.58	0.12	0.84	0.38	0.43	neg.
9 Gi.	0.05	0.02	0.04	0.08	0.03	0.06	neg.
10 Hag.	8.7	7.9	18.7	8.4	4.0	300	neg.
11 Bu. ¹	21.0	38.0	20.0	8.4	6.0	21	neg.
12 Ly.	420	190	300	420	190	300	neg.
13 Hat. ¹	42	11.5	100	8.4	3.3	40	neg.
14 Pe.	56	115	100	420	230	100	neg.
Mean ± SD	50.4 ± 113	29.8 ± 55.2	51.9 ± 81.9	66.3 ± 150.2	33.9 ± 75.3	57.9 ± 106	
<i>Large local reactions</i>							
15 Ap.	21	19	81	84	38	30	neg.
16 Ag.	10.5	0.07	3.7	42	0.19	3.0	neg.
17 Su. ¹	28	9.5	80	8.4	190	60	neg.
18 Ho.	2.6	0.06	0.46	0.08	0.55	0.06	neg.
19 Za.	220	340	300	220	340	300	neg.
20 Wi.	10.5	0.35	0.94	4.2	0.46	0.6	neg.
Mean ± SD	48.8 ± 84.4	61.5 ± 36.5	77.7 ± 116	59.78 ± 84.69	91.8 ± 140.8	65.6 ± 117.2	
<i>Controls</i>							
1 Wa.	ND	ND	ND	420	4.0	60	neg.
2 Az.	ND	ND	ND	220	340	300	neg.
3 Na.	ND	ND	ND	420	190	300	neg.
4 Fo.	ND	ND	ND	84	4.0	6.0	neg.
5 Se.	ND	ND	ND	8.4	23	60	neg.
6 Fa.	ND	ND	ND	84	230	60	neg.
7 On.	ND	ND	ND	420	230	300	neg.
8 La.	ND	ND	ND	420	46	300	neg.
9 Go.	ND	ND	ND	420	230	300	neg.
10 Ne.	ND	ND	ND	84	46	60	neg.
Mean ± SD				258 ± 178.2	134.3 ± 122.4	174.6 ± 133.2	

ND = Not determined.

¹ Had previously received immunotherapy.

comparison of WBE and venom skin test EPs utilized the relative change in EP threshold by taking 1 patient as a reference point (the one with the lowest venom EP). The relative 'fold' change for individuals in the various groups compared to that patient for each of the antigens was then evaluated using the *t* test. The Sign test was used for analysis of data in table IV.

Results

With twofold venom skin testing, the mean MRDs were 0.33 μ g for YJ, 1.84 μ g for Pol and 0.61 μ g for WFH (table IIa). The MRDs with tenfold testing were similar. The control MRDs were 2.43 μ g for YJ, 3.26 μ g for Pol and 2.27 μ g for WFH. The lowest twofold MRD in 11 of 14 clinically sensitive patients was to YJ venom, this figure being 8 of 14 with tenfold venom testing. WBE twofold skin testing showed MRDs of 50.4 PNU for YJ, 29.8 PNU for Pol and 51.9 PNU for WFH (table IIb). Tenfold dilution testing was again similar. Control MRDs were 258 PNU for YJ, 134.3 PNU for Pol and 174.6 PNU for WFH.

Comparison of mean MRDs is given in table III for each insect extract. Skin testing with WBE and venom distinguished between the normal control and systemic reaction group except for twofold Pol venom. There was no significant difference by *t* test analysis between twofold and tenfold MRDs with either WBE or venom antigens.

T test comparisons of WBE EP versus venom EP testing showed no statistical difference for YJ (table III). On the other hand, the same comparisons for Pol and WFH antigens showed significant differences in each instance.

The range of control skin test values was large enough to overlap considerably with

patient values so that even though the groups were clearly different, an individual's MRD could be considered significant only if it was below the lowest control EP for a given antigen. A significantly greater number of patients considered clinically hypersensitive by our previously stated criteria were detected by YJ venom skin testing as compared to YJ WBE skin testing (table IV). The detection of patients considered clinically hypersensitive was not significant with Pol or WFH venom or WBE skin testing. Most of the patients with systemic reactions were thought to have suffered YJ stings. Since patients cannot always reliably identify an offending insect, the lowest MRDs obtained for each patient, regardless of which antigen elicited it, were also analyzed. These MRDs were designated as the 'least EP' (table IV). Detection of patients considered clinically hypersensitive was significant with venom testing using the 'least EP'. This result is similar to that with YJ venom skin testing.

Among the 6 patients who experienced exceptionally large local reactions, 50% or less showed a positive skin test with any of the antigens used (table IV). Only 1 patient had a positive RAST.

Radioallergosorbent Test

7 of 14 patients considered clinically hypersensitive had a positive RAST to an insect venom. All of these patients were positive to YJ venom. 1 patient was positive to all three venoms (table Va). The occurrence of a positive venom RAST in the patient group with a history of systemic reactions was significantly different from the control group by *t* test ($p < 0.01$). All controls and all patients with large local reactions had a negative venom RAST. WBE RAST deter-

Table III. Student t test analysis of WBE and venom skin test EP in patients with systemic reactions and control

Comparison of minimum reactive doses	p		
	YJ	pol	WFH
WBE controls ¹ vs. WBE patients ² twofold	0.005	< 0.01	< 0.025
WBE controls vs. WBE patients tenfold	< 0.01	< 0.025	< 0.05
WBE patients twofold vs. WBE patients tenfold	> 0.50	> 0.56	> 0.50
Venom controls ¹ vs. venom patients ² twofold	< 0.001	< 0.10	< 0.005
Venom controls vs. venom patients tenfold	< 0.001	< 0.01	< 0.01
Venom patients twofold vs. venom patients tenfold	> 0.50	< 0.40	> 0.50
Venom patients twofold vs. WBE patients twofold	> 0.50	0.001	< 0.02
Venom patients tenfold vs. WBE patients tenfold	< 0.20	< 0.001	< 0.02

¹ WBE controls; venom controls: 10 patients.² WBE, EP and venom EP two- and tenfold: 14 patients with systemic reactions.**Table IV.** Skin test and RAST detection of patients clinically sensitive by history

	YJ	Pol	WFH	'Least EP'
<i>Systemic reactors (n = 14)</i>				
Venom skin test				
Twofold	12/14 ¹	9/14	7/14	12/14 ¹
Tenfold	12/14 ¹	8/14	7/14	
WBE skin test				
Twofold	8/14	6/14	6/14	7/14
Tenfold	6/14	7/14	5/14	
Venom RAST	7/14	1/14	1/14	
<i>Large local reactions (n = 6)</i>				
Venom skin test				
Twofold	3/6	2/6	1/6	3/6
Tenfold	3/6	3/6	3/6	
WBE skin test				
Twofold	1/6	3/6	3/6	3/6
Tenfold	2/6	3/6	3/6	
Venom RAST	0/6	1/6	0/6	

¹ p < 0.05; probability that detection of clinically sensitive patients is due to chance (all other above values p > 0.05).

Table Va. Venom RAST - % total cpm bound

	YJ		Pol		WFH	
Mean control: run I, %	3.8		2.0		2.1	
Total cpm bound: run II, %	3.1		2.3		2.0	
	total cpm bound	clinical 'positivity'	total cpm bound	clinical 'positivity'	total cpm bound	clinical 'positivity'
<i>Systemic reactions</i>						
Run I						
Me.	15.5	+	4.6	+	13.2	+
Bi.	6.2	+	2.4	neg.	3.1	neg.
Bs.	5.3	+	2.4	neg.	2.4	neg.
Gi.	6.3	+	2.6	neg.	3.0	neg.
Hag.	7.7	+	2.0	neg.	2.0	neg.
Ly.	3.6	neg.	2.4	neg.	2.3	neg.
Hat.	4.2	neg.	2.1	neg.	1.9	neg.
Run II						
Ph.	6.2	+	3.6	neg.	3.4	neg.
Gr.	5.6	+	3.0	neg.	2.9	neg.
Co.	4.6	neg.	2.4	neg.	3.0	neg.
Bu.	4.1	neg.	3.0	neg.	2.4	neg.
Eo.	4.1	neg.	3.0	neg.	2.0	neg.
Ba.	3.7	neg.	2.4	neg.	2.3	neg.
Pe.	3.2	neg.	2.4	neg.	2.1	neg.
<i>Large local reactions</i>						
Run I						
Ap.	2.8	neg.	2.7	neg.	2.0	neg.
Za.	4.0	neg.	2.1	neg.	1.9	neg.
Su.	4.2	neg.	2.3	neg.	2.3	neg.
Run II						
Ag.	4.1	neg.	3.7	neg.	3.2	neg.
Wi.	4.2	neg.	3.0	neg.	2.8	neg.
Ho.	4.0	neg.	2.5	neg.	1.9	neg.

minations were uniformly negative (table Vb). RAST-negative patients had a mean interval of sting to acquisition of serum for RAST of 6 years, all but 1 having an interval of 1 year or more. RAST-positive patients had a mean interval from time of sting to RAST of 10.3 months, all but 1 interval being 1 year or less.

Comparison of Skin Testing and RAST

Detection of patients considered clinically hypersensitive was, in the case of YJ venom RAST, similar to results with WBE skin testing (table IV). Such detection was significantly less compared to YJ venom skin testing. The results of venom RAST or skin testing with the other two venoms were not

Table Vb. WBE RAST – % total cpm bound

	YJ		Pol		WFH	
Mean control: run I, %	1.5		1.7		1.7	
Total cpm bound: run II, %	1.5		1.5		1.5	
	total cpm bound	clinical 'positivity'	total cpm bound	clinical 'positivity'	total cpm bound	clinical 'positivity'
<i>Systemic reactions</i>						
Run I						
Me.	3.1	neg.	2.0	neg.	2.4	neg.
Bi.	1.8	neg.	1.3	neg.	1.8	neg.
Bs.	1.8	neg.	1.7	neg.	1.9	neg.
Gi.	2.1	neg.	2.1	neg.	2.4	neg.
Hag.	1.5	neg.	1.7	neg.	1.7	neg.
Ly.	1.5	neg.	1.5	neg.	1.7	neg.
Hat.	1.5	neg.	1.4	neg.	1.8	neg.
Run II						
Ph.	2.1	neg.	1.9	neg.	2.3	neg.
Gr.	2.0	neg.	1.8	neg.	2.2	neg.
Co.	2.2	neg.	1.9	neg.	1.9	neg.
Bu.	1.9	neg.	2.1	neg.	2.1	neg.
Eo.	2.0	neg.	2.3	neg.	1.4	neg.
Ba.	1.3	neg.	1.2	neg.	1.3	neg.
Pe.	1.7	neg.	1.4	neg.	1.6	neg.
<i>Large local reactions</i>						
Run I						
Ap.	1.5	neg.	1.7	neg.	1.7	neg.
Za.	1.5	neg.	1.5	neg.	1.8	neg.
Su.	1.5	neg.	1.6	neg.	1.8	neg.
Run II						
Ag.	1.7	neg.	2.1	neg.	1.9	neg.
Wi.	2.2	neg.	2.3	neg.	2.5	neg.
Ho.	1.5	neg.	1.4	neg.	1.5	neg.

statistically significant in terms of number of patients detected.

Discussion

To date, there are no unequivocal objective tests to substantiate that the symptoms

experienced by a patient following a Hymenoptera sting are the result of an immunological reaction. Some of the usually accepted symptoms that characterize type I anaphylactic reactions are nonspecific and could be secondary to other mechanisms. *In vitro* histamine release has been proposed as a criterion for resolving this problem [8],

however, some nonsensitive subjects show significant histamine release from basophils with Hymenoptera venoms [15] while some patients positive by skin test fail to show basophil histamine release [16]. In this study venom skin-testing detected more patients suspected of being clinically hypersensitive than did either the RAST or whole-body skin testing (table IV). This finding is in accord with that of *Zelevnick et al.* [15] who were able to separate clearly sensitive from nonsensitive individuals on the basis of skin testing. The minimal reactive concentration eliciting a positive reaction in that study was very similar to what we obtained, if differences in expressing minimal reactive dose are taken into account. Others have also found that skin testing with WBE did not consistently differentiate sensitive from nonsensitive patients [8, 15]. Data in table III comparing venom and WBE EPs suggest, however, that WBE may have some usefulness in detecting clinically hypersensitive patients since as a group, venom and WBE EPs were not statistically different for YJ antigen. This was not the case for Pol or WFH. On review of patient histories and from data in table IV, it was thought that most clinically hypersensitive patients in our study were YJ sensitive.

The present study suggests that the RAST technique is not as sensitive as venom skin testing in detecting clinical sensitivity although the RAST appears to be of some use. *Reisman et al.* [10] felt that the RAST was useful in diagnosing stinging insect hypersensitivity; however, they compared this technique to WBE skin testing only. In addition, a number of clinically sensitive patients in that study (at least 17%) had a negative RAST. *Hoffman and Shipman* [17] found a positive RAST in 92% of 24 pa-

tients with systemic reactions to bee sting. All of these patients were stung within 4 months of obtaining serum for RAST. In contrast, RAST-negative patients in our study had a considerably longer mean interval of sting to acquisition of serum for RAST. Such variation in time intervals may explain the difference in RAST results between the two studies. Technical modification of the RAST might increase its sensitivity, but the method used in our study is the one in general use.

Skin testing and RAST results in patients who experienced unusually large local reactions after a sting were inconclusive. The skin testing results suggest that some might be subject to clinical hypersensitivity but the number of patients is too small for analysis. *Reisman et al.* [10] found that 12 of 14 patients with large local reactions had a positive RAST to at least one of three venoms. One might suppose that such patients represent a transition from a normal to a hypersensitive state and that patients who have abnormal venom skin tests may represent those at greater risk following subsequent stings. Perhaps they should be treated. Only prospective studies, in which large numbers of such patients are followed up, can answer this question.

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