

A critical evaluation of RAST to venoms of Hymenoptera

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Summary

RAST to venoms were done on 108 sera. Positive RAST to one or more venoms of Hymenoptera found in 51% (41/80) patients with a generalized reaction to the sting of Hymenoptera and in 7% (2/28) of normal controls were critically evaluated. RAST determinations for each sera were done in duplicate and results averaged. The laboratories were not told which sera belonged to patients with allergy to Hymenoptera and which belonged to controls. In ten patients, one half of the original sera were saved and RAST to venoms were repeated approximately 1½ years later. Of our positive RASTs, 49% (20/41) had positives to more than one type of venom. The most frequent positive RAST was to yellow jacket followed by hornet, wasp, and honey bee. A high degree of cross-reactivity occurred between venoms of hornet, wasp, and yellow jacket. The frequency of positive RAST was similar in pre-treatment and post-treatment sera from patients on immunotherapy with whole body extract. Specific IgE (RAST) results to venoms did not correlate with the degree of clinical severity of the sting. However, IgG anti-venom antibodies were not considered. Elevated RAST titres were associated with increased total IgE levels in sera of non-atopic patients. A positive RAST to venoms is frequently found in sera of patients stung within 5 years. RAST scores of 2 to 4 were remarkably reproducible, while scores of 1 were not consistently reproducible. RAST results should be interpreted in conjunction with the clinical history.

Introduction

In our previous study (Settipane *et al.*, 1980) on anaphylactic reactions in asthmatic patients, our RAST data on venoms demonstrated that asthmatics did not have a significantly greater frequency of positive RAST to venoms than non-asthmatics. The significantly greater frequency of acute bronchospasm as a result of an insect sting in asthmatics was probably due to an inherent sensitivity to histamine or other allergic

mediators. In our study on the natural history of Hymenoptera allergy, (Settipane & Chafee, 1979), we used some of our RAST data to demonstrate that the results of RAST to venoms correlated with clinical signs and symptoms of a previous sting. In this report we will evaluate our RAST data on insect venoms in greater detail. We will determine the relationship of pre-treatment and post-treatment immunotherapy with whole body extract, cross reactivity between venoms of Hymenoptera, total IgE, time interval since last sting, and severity of clinical symptoms to results of RAST using venoms of various Hymenoptera. We will also determine if RAST scores to venoms are reproducible.

Materials and methods

Clinical data on our eighty patients with a generalized reaction to Hymenoptera and twenty-eight normal controls have been reported previously (Settipane *et al.*, 1980). As defined in past reports (Settipane *et al.*, 1980; Settipane & Chafee, 1979; Settipane *et al.*, 1978), an allergic reaction to Hymenoptera sting is defined as generalized hives/angioedema (grade II), acute dyspnoea (grade III), shock or a degree of syncope (grade IV), occurring shortly after the sting. Patients with local reactions, regardless of size (grade I), were not included in this study (Table 1).

Table 1. Classification of reaction to Hymenoptera stings

Grade I	Local swelling only
Grade II	Generalized hives/angioedema
Grade III	Dyspnoea (bronchospasm)
Grade IV	Shock or a degree of syncope

Each grade of reaction usually includes symptoms of the previous lower grades.

In eighty patients with allergy to Hymenoptera stings, and in twenty-eight normal controls (without generalized or large local reactions to Hymenoptera stings), blood was drawn and sera frozen and stored. These sera were later sent in a frozen state to private laboratories* for total and specific IgE determinations to venoms of honey bee, yellow jacket, hornet, wasp and to phospholipase A. These tests were done in duplicate and results were averaged. The laboratories were not told which sera belonged to the normal controls and which belonged to those with allergy to Hymenoptera. The venom antigens used by these laboratories have been previously described. (Settipane *et al.*, 1980). Results from the RAST data were reported using the standard Pharmacia scoring system. Serum IgE was determined by the PRIST method.

Results

Positive RAST scores to one or more venoms were found in 51% (41/80) of patients with a definite history of a generalized reaction to a Hymenoptera sting and in 7% (2/28) of normal controls with no history of generalized or large local reactions to

* Pharmacia Diagnostics, Piscataway, N.J.; Genatom, East Orange, N.J.; and Aid Service Corporation, Princeton, N.J.

Hymenoptera sting. Of these forty-one positive RASTs, 49% (twenty) had positive RAST to more than one type of venom. There was no difference in multiple positive RAST scores in sera drawn before immunotherapy and sera drawn after initiation of whole body extract immunotherapy (Table 2). The most frequent positive RAST was to yellow jacket, followed by hornet, wasp and honey bee (Table 3). There were eleven sera with positive RAST to honey bee venom and five of these also had positive RAST to phospholipase A. All sera with positive RAST to phospholipase A also had positive tests to honey bee venom. Sera with positive RAST to venoms of hornet and wasp also were positive to other venoms. Sera with a positive RAST to hornet venom was associated with a positive RAST to yellow jacket, and sera with a positive RAST to wasp was associated with a positive RAST to both yellow jacket and hornet venom.

Those patients with positive RAST to venoms did not have a more severe grade of reaction on their last previous sting than those with negative RASTs (Table 4). In addition, an increased titre of positive RAST (score of 2 or greater) was not associated with an increased grade of clinical severity, and was similar in pre- and post-treatment sera (whole body extract).

An increase in RAST scores was associated with an increase in total serum IgE. In Table 5, sera from patients with asthma/allergic rhinitis were not included because these patients are ordinarily expected to have an elevated serum total IgE because of their atopic background. Therefore, in Table 5, the serum total IgE reflects only the specific IgE to venoms. The mean total IgE in negative RAST and a 1 score positive RAST to venoms is similar. Serum with a RAST score of 2 had a mean total IgE that was about double that of RAST score 1. A similar doubling in mean total IgE occurred when the RAST score increased from 2 to 3.

A great majority of our sera were drawn within 2 years of the last insect sting. However, five of the sera were drawn within 5 years of the last sting and four of these had a positive RAST. One other serum drawn 6 years after the last sting had a negative RAST. There was essentially no difference in results between pre- and post- whole body immunotherapy sera when comparing the interval of the last sting to the time when blood was drawn.

In normal controls there were two sera with positive RAST: one to wasp venom alone, and the other to honey bee, phospholipase A, wasp, hornet and yellow jacket. The clinical significance of these positive tests in our controls is unknown since these controls have not been re-stung.

RAST tests to venoms in ten sera were repeated approximately 1½ years later by saving some of the original sera in frozen state and sending them to the same laboratory in a blinded manner. RAST scores of 2–4 were remarkably reproducible (6/6) while in four sera, RAST scores of 1 were not consistently reproducible.

Discussion

Positive specific IgE to one or more venoms in a significant number of patients with generalized reactions have been reported by several investigators. The Johns Hopkins group (Hunt *et al.*, 1976) reported that 13% of their patients in one study had multiple positive skin tests to various insect venoms. In another study, (Kern *et al.*, 1976), it was reported that thirteen out of eighteen patients demonstrated significant histamine release to three or more venoms. Six out of these thirteen patients with multiple positive venom tests had not received any previous whole body extract immunotherapy and seven had received previous whole body immunotherapy. Reisman *et al.*

Table 2. Positive RAST to Hymenoptera venoms in patients with generalized reactions to Hymenoptera

Sera	Honey bee/ phospholipase A		Yellow jacket		Hornet		Wasp		Positive RAST to more than one venom	
	Total	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No.
Pretreatment	25	7	28	25	100	10	40	6	24	13
Post treatment	16	4	25	14	88	6	38	5	31	7
Total	41	11	27	39	95	16	39	11	27	20
										49

Table 3. Forty-one patients with positive RAST in patients with generalized reactions to Hymenoptera: cross reaction between venoms

Insects	Positive RAST: one or more venoms		Positive RAST: one venom only		Positive RAST: multiple venoms	
	No.	Percentage with positive RAST ($n=41$)	No.	Percentage of positive RAST per insect	No.	Percentage of positive RAST per insect
Yellow jacket	39	95	19	49	20	51
Hornet	16	39	0	0	16	100
Honey bee/phospholipase A	11	27	2	18	9	82
Wasp	11	27	0	0	11	100

Table 4. Grade of Hymenoptera reaction and positive RAST to one or more venoms.

	Grand total	Grade I*			Grade II			Grade III/IV			P value
		Total	Positive RAST	Percentage	Total	Positive RAST	Percentage	Total	Positive RAST	Percentage	
Pre-treatment	51	3	0	0	26	14	53.8	22	11	50.0	n.s.
Post-treatment	29	13	10	76.9	9	3	33.3	7	3	42.9	
	80	16	10	62.5	35	17	48.6	29	14	48.3	

* Grade I reactions occurred on re-sting. All had generalized reactions on previous stings.

† n.s.—Not significant.

Table 5. Relationship of RAST scores and total IgE in a non-atopic population*

Highest RAST scores to venoms†	Total patients	Mean IgE u/ml
Negative	28	132.9
Score 1	18	135.0
Score 2	13	318.6
Score 3	4	644.0
Total	63*	

* 16 atopic patients (those with asthma and/or rhinitis) were excluded.

Another patient was excluded because a total IgE was not done.

† Standard Pharmacia scoring system.

(1976) reported that 37% of his patients had positive RAST to multiple venoms. In that study, those investigators also stated that venom-specific IgE was not significantly affected by previous treatment with whole body extract. Busse & Yunginger (1978) reported that 24% of their patients had positive RAST to multiple venoms, and that 44% of their total patients with generalized reaction to insect stings had a positive RAST. Our study is in full agreement with those past reports in that 49% of our patients with positive RAST had multiple positive tests to venoms. Similar to Busse and Yunginger (1978), 51% of our total population with generalized reactions to insect sting had a positive RAST while only 7% of our normal controls had positive RAST. Serum RAST determinations are helpful in identifying the allergic patient from the normal control.

Our data also suggest that a great deal of cross-reactivity exists among the venoms of Hymenoptera (Table 3). In our part of the country, yellow jacket is the most common insect whose sting causes a generalized reaction. In addition, it is apparent the venoms of yellow jacket, hornet and wasp appear to have similar antigenic components.

Our data did not demonstrate any correlation between severity of clinical grade of reaction and positive RAST scores. These results conform with previous reports (Lessof, Sobotka, Lichtenstein, 1976; Valentine *et al.*, 1976) in that improvement may be associated with high levels of IgG anti-venom antibody rather than specific IgE antibody. In addition, similar to Reisman *et al.* (1976), we found no significant difference between the pre- and post-treatment sera for specific IgE when whole body extract was used for immunotherapy.

A positive RAST to venoms without any other manifestation of atopy such as asthma and allergic rhinitis can significantly effect the level of total serum IgE. A 3+ RAST score to venoms can increase the total serum IgE approximately five-fold (Table 5). It is well accepted that atopic asthma and allergic rhinitis are also associated with an elevated serum total IgE (Spitz *et al.*, 1972). Our data support the concept that an excellent screening test for any type of active clinical allergy is an elevated total serum IgE.

Our data regarding intervals between the last sting and the time when blood was drawn for RASTs indicated that it is possible to obtain a positive RAST as long as 5 years after the insect sting. Hunt *et al.*, (1978), reported positive skin tests to venoms as long as 3–18 years after the last sting. However, our data (Settipane & Chafee, 1979) on

clinical improvement on a re-sting suggests that the frequency of positive RAST may decrease when the time interval is over 5 years from the last sting. Reisman & Arbesman (1975) have shown that false negative RASTs may be present for several days after a sting – the anergic period. Therefore, it is important to evaluate RAST results with the time interval of the last sting.

We were unable to compare skin tests with RAST to venoms. When this study was completed, venom skin test material was not available on a commercial basis. However, we feel that RAST to venoms is an important adjunct in the diagnosis and treatment of generalized reactions to the sting of insects.

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