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Natural history of allergy to Hymenoptera

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Summary

One hundred and nineteen patients who had a generalized reaction to a bee sting and who subsequently had a history of being re-stung before desensitization were studied. The reaction, in these 119 patients was as follows: 44·5% had an improved grade of reaction, 42·9% had the same grade of reaction and 12·6% had a worse grade of reaction. Of these 119 patients, 39·5% had only a local reaction to their re-sting. Those patients who were re-stung within 2 weeks (anergic period) or over 5 years after a generalized reaction to a sting had significantly improved response. Results of pretreatment RAST to venoms of hornet, yellow jacket, wasp, honey bee and to phospholipase A appeared to correlate with the clinical signs and symptoms of the previous sting in 75% of cases.

Introduction

Double blind controlled studies which evaluate desensitization treatment in patients allergic to bee stings are rare, for investigators are reluctant to withhold treatment which they consider beneficial. One useful parameter of evaluating desensitization treatment is to consider those patients who experienced a generalized reaction to a sting and who were subsequently re-stung before desensitization treatment. This approach is not as satisfactory as the double blind controlled method, but may contribute to our knowledge of the natural history of allergy to insects. In this investigation we attempt to evaluate re-sting reactions in those patients who had an earlier generalized reaction to an insect sting and who were subsequently re-stung before immunotherapy was instituted.

Materials and methods

Patients with a preceding generalized allergic reaction to stings by insects (wasp, yellow jacket, hornet, and honey bee) were evaluated for a history of a subsequent sting occurring before desensitization treatment. An allergic reaction to bee sting is defined

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as generalized hives/angioedema (Grade II), acute dyspnoea (Grade III), or a degree of syncope (Grade IV) occurring shortly after the sting (Settipane, Klein & Boyd, 1978). Local reactions, regardless of size, were classified as Grade I and were not included in this study. Toxic reactions from large numbers of simultaneous stings were also excluded.

There were 119 patients who had a preceding generalized allergic reaction to stings of insects followed by a subsequent sting before desensitization was initiated. Information from at least 42 (35·3%) of these patients was obtained by direct personal interviews, and information from other patients was obtained by reviewing consecutive records from private offices and from the Rhode Island Hospital Allergy Clinic. When charts were incomplete, an attempt was made to contact these patients. If pertinent information was still not available, these cases were not included in our study. All questionable cases of sting reactions were also excluded.

In evaluating re-sting reactions a change from the previous generalized reaction was considered only if the patient's new symptoms warranted a change in grade. For example, if a patient initially described dyspnoea (Grade III) or syncope (Grade IV) with the preceding bee sting and experienced a local reaction (Grade I) or generalized hives only (Grade II) with a subsequent re-sting, the patient was considered improved since the initial symptoms had changed from a Grade III or IV to a Grade I or II. Improvement or worsening of symptoms within the same grade were not considered as a change. For example, if a patient experienced generalized hives with the initial sting and experienced only a milder case of generalized hives in the subsequent sting, both sting reactions were still classified as Grade II and were not considered as a changed reaction. Patients were counted only once per category regardless of the number of re-stings recorded. The data used was the last re-sting response that followed a generalized reaction before desensitization treatment. If the last several re-stings resulted in local reactions (Grade I), only the first Grade I response was considered. By this procedure we attempted to minimize the influence of a few patients with many re-stings.

In categorizing these patients, a diagnosis of asthma was accepted if symptoms consisted of clinically reversible signs of wheezing, shortness of breath and cough on a recurrent basis, not due to any other disease. A diagnosis of rhinitis was accepted if symptoms consisted of recurrent nasal stuffiness, rhinorrhoea and frequent sneezing on a seasonal or non-seasonal basis. Cases of infectious rhinitis were excluded from the rhinitis category. Patients with both asthma and rhinitis were classified as asthma and only those patients with rhinitis alone were classified as rhinitis. For this study, atopy is defined as having a past or present history of asthma or rhinitis.

In twelve of these patients with bee sting allergy who experienced a re-sting prior to desensitization, blood was obtained before desensitization treatment was begun. All bloods were drawn within 3 years from the last sting. Sera was frozen, stored and later sent in a frozen state to private laboratories* for specific IgE determinations to venoms of honey bee, yellow jacket, hornet, wasp and a phospholipase A.

Results

Of these 119 patients who experienced a preceding generalized reaction to stings by insects followed by a re-sting before desensitization treatment was begun, ninety-four (79·0%) were males and twenty-five (21·0%) were females. The age range on the initial

* Pharmacia Diagnostics, Piscataway, New Jersey; and Genatom, East Orange, New Jersey.

generalized reaction to the bee sting was 2–70 years with a median age of 21·9 years. Fifty-six (47·1%) were 12 years or younger. Of these 119 patients, seventeen had two or more re-stings before desensitization and of these, seven patients had three or more re-stings before desensitization. Patients with multiple re-stings on different occasions had similar responses as those with only one re-sting. The frequency of atopy (asthma/rhinitis) was 26·9%, 12·6% with asthma, and 14·3% with rhinitis alone (Table 1).

Following a re-sting, these 119 patients had the following reactions: fifty-three (44·5%) had an improved grade of response of which forty-seven (39·5%) of the 119 patients had only a local reaction (Grade I). Fifty-one patients (42·9%) experienced the same grade of reaction and fifteen (12·6%) had a worse reaction (Table 2). The change in grade on re-sting did not appear to depend on the previous grade of reaction. Individuals 12 years or younger had similar re-sting responses. The re-sting responses in those patients with asthma and rhinitis were similar to those without asthma/rhinitis.

The interval between the last generalized reaction to a sting and a subsequent re-sting significantly affected the clinical response. Those patients who had been re-stung within 2 weeks or over 5 years from the last generalized reaction had significantly improved grades of reaction compared to those who were re-stung between 2 weeks and 5 years after a generalized reaction to a sting. None of the patients re-stung within 2 weeks of a generalized reaction had a worse response. Only one out of nineteen (5·3%) of those re-stung over 5 years from the last generalized reaction had a

Table 1. Hymenoptera allergy: 119 patients re-stung before desensitization

Males	94	79·0%
Females	25	21·0%
Mean age (yrs)	21·9	
Age range (yrs)	2–70	
Age 12 or younger	56	47·1%
Asthma	15	12·6%
Rhinitis (alone)	17	14·3%
Non atopic	87	73·1%

Table 2. Hymenoptera allergy: re-sting response before desensitization

	No. of patients	
Re-sting response	Total	%
I. Better grade	53	44·5
a. local reaction only	(47)	(39·5)
II. Same grade	51	42·9
III. Worse grade	15	12·6
Total	119	

Table 3. Effect of time on re-sting reactions

Time interval	Total patients	Improved No.	Improved %	Improved *P* value	Worse No.	Worse %	Worse *P* value
2 weeks or less	16	10	62·5		0	0	
				⩽0·033			
Over 2 weeks to 5 years	74	25	33·8		14	18·9	
				⩽0·020			NS
Over 5 years	19	12	63·2		1	5.3	
Unknown	10						
Total	119						

worse response. In seventy-four patients re-stung between 2 weeks and 5 years, fourteen (18·9%) had a worse reaction (Table 3).

RAST tests to venoms of honey bee, yellow jacket, hornet, wasp and phospholipase A were done on twelve sera drawn before desensitization treatment was initiated. Five patients had one or more positive RAST and all of these patients had a generalized reaction (Grade II–IV) preceding the time when blood was drawn. Seven patients had negative RASTS and three of these seven had only local reactions preceding the time that blood was drawn, and in another one of these patients, blood was drawn during the anergic period, one week after the sting. RAST results appear to correlate with the preceding clinical signs and symptoms to a sting in nine out of twelve patients (75%).

Discussion

The major problem with a re-sting study is that patients with a specific sensitivity to certain species of Hymenoptera may be re-stung by another non-reacting species and may not experience a generalized reaction with the venom of this other species. Most studies on the efficacy of treatment with Hymenoptera extracts attribute improvement that occurs with a re-sting to the therapy without regard to the fact that a different insect may be responsible for that re-sting. This factor may account for some of the less severe reactions observed when re-stung. However, when comparing the improvement rates in various categories in our study, the frequency of stings from non cross-reacting insects probably are about the same for each category and, therefore, may not cause the differences found in our comparisons.

It is also possible that many individuals who had a preceding generalized reaction to a sting and who experienced only local reactions to a subsequent re-sting are less likely to seek medical attention. Therefore, our observed rate of improvement following a re-sting may actually be increased if a non-biased segment of the general population had been evaluated rather than considering only those individuals who had sought an allergist's opinion.

A review of the literature reveals few reports on re-sting reactions before treatment in patients who had a preceding generalized reaction. The Insect Allergy Committee of the American Academy of Allergy reported in 1965 that 39·2% (40/102) improved when re-stung before desensitization. Another report by this committee (Torsney,

1968) showed that the improvement rate on being re-stung before desensitization was 67·5% (164/243). However, this data may be criticized as follows: it was highly selected (pooled data by many contributors throughout the country); it considered subjective feelings of improvement within the same grade rather than an actual improved grade of reaction; and it considered large local reactions as the preceding allergic reaction to a re-sting. Brown & Bernton (1970) reported an improvement rate for re-sting before desensitization of 92·9% (39/42). These patients were also highly selected in that only those patients with equivocal skin tests to Hymenoptera extract were considered. In addition, questionable symptoms, such as headache and fever were used as evidence of allergy to Hymenoptera. Our study was done in one geographic area, has used strict criteria for generalized reaction to stings, and has evaluated subjective feelings by considering only a better grade of reaction as improvement.

Similar to our past studies (Settipane, Newstead & Boyd, 1972; Settipane *et al.*, 1978) the frequency of asthma/rhinitis in our population of 119 patients with re-stings is 26·9% and corresponds to what one expects to find in the general population. When comparing re-sting reactions, those patients with asthma or rhinitis did not appear to differ from other patients in this study.

The time interval between the last generalized reaction to a sting and a subsequent re-sting may be significant in determining the rate of improvement. Those patients re-stung within 2 weeks following a generalized reaction to sting may be in an anergic period (Reisman & Arbesman, 1975; Findlay *et al.*, 1977) which would explain in our study why those patients who were re-stung within 2 weeks had a significantly improved response compared to those re-stung over 2 weeks to 5 years. Those re-stung over 5 years later may have a naturally occurring decrease in the specific IgE to venoms and this phenomenon might explain why these patients have a significantly increased improvement with a re-sting.

Our pre-treatment RAST results correlate with the previous sting reaction in 75% of the cases. Those who had a generalized reaction to the sting before blood was drawn usually had a positive RAST, while those who had a local reaction to a previous sting or were in the anergic period usually had a negative RAST. False negative and false positive reactions to RAST have been reported (Müller, Speiss & Roth, 1977). In our data the results of RAST appear consistent with the appropriateness of our grading system for systemic reactions to insect stings.

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References

BROWN, J. & BERNTON, H.S. (1970) Allergy to Hymenoptera v. clinical study of 400 patients. *Archives of Internal Medicine*, **125**, 665.

FINDLAY, S.R., GILLASPY, J.E., LORD, R., WEINER, L.S. & GRANT, J.A. (1977) Polistes wasp hypersensitivity: diagnosis by venom-induced release of histamine *in vitro*. *Journal of Allergy and Clinical Immunology*, **60**, 230.

INSECT ALLERGY COMMITTEE OF THE AMERICAN ACADEMY OF ALLERGY (1965) Insect-sting allergy: questionnaire study of 2606 cases. *Journal of the American Medical Association*, **193**, 115.

MÜLLER, U., SPEISS, J. & ROTH, A. (1977) Serological investigations in Hymenoptera sting allergy: IgE and haemagglutinating antibodies against bee venom in patients with bee sting allergy, bee keepers and non-allergic blood donors. *Clinical Allergy*, **7**, 147.

REISMAN, R.E. & ARBESMAN, C.E. (1975) Stinging insect allergy: current concepts and problems. *Pediatric Clinics of North America*, **22**, 185.

SETTIPANE, G.A., KLEIN, D.E. & BOYD, G.K. (1978) Relationship of atopy and anaphylactic sensitization: a bee sting allergy model, *Clinical Allergy*, **8**, 259.

SETTIPANE, G.A., NEWSTEAD, G.J. & BOYD, G.K. (1972) Frequency of Hymenoptera allergy in an atopic and normal population. *Journal of Allergy & Clinical Immunology*, **50**, 146.

TORSNEY, P.J. (1968) Allergic reactions to insect stings. *New York State Medical Journal*, **68**, 2765.

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