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Hymenoptera Stings and Serum Venom-specific IgE in Japanese Pest-control Operators

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Abstract

Pest-control operators represent a high occupational risk for Hymenoptera sting and a possibility of Hymenoptera allergic reactions, but the information is not well documented. A history of Hymenoptera stings was found in 118 (59.0%) of 200 Japanese pest-control operators. To evaluate the details of Hymenoptera stings and the factors associated with venom-specific IgE level which indicates Hymenoptera allergy, a questionnaire was administered and serum venom-specific IgE levels were measured in 105 subjects selected from 118 operators. The number of past stings was a mean of 3, and in most cases, they had been stung at only one site on the hand or the head and neck. Systemic reactions to Hymenoptera stings were also less frequent among them (5/105). Venom-specific IgE (to a yellow jacket, a wasp, and a honeybee) was measured by the CAP system, and it was found to be positive in 31.4% of the 105 subjects. The frequency of positive CAP was significantly associated with the following factors: the total serum IgE level ($P<0.001$), the time interval from the last sting-incident ($P<0.001$), the number of past stings ($P<0.05$), the most recent clinical symptoms ($P<0.05$), and an individual atopic history ($P<0.05$). Among these 5 factors, the former 4 factors were shown to influence the venom-specific IgE titer in the multiple-regression analysis using a forward-stepwise technique (multiple $R=0.708$, adjust $R^2=0.482$, $P<0.001$). In particular, the influences of the total serum IgE level and the time interval were strong. These findings indicate that the frequency of Hymenoptera stings in pest-control operators is not as high as in beekeepers or forestry workers, and that venom-specific IgE is affected mainly by the total serum IgE level and the time interval from the last sting-incident.

Key words: Hymenoptera stings, Venom-specific IgE, Pest-control operators

Introduction

Hymenoptera stings are accidental events and the related allergic reactions often cause serious medical problems.[1] The diagnostic indicators of Hymenoptera hypersensitivity are based on immunological reactivity, as measured by the presence of venom-specific IgE, and clinical sensitivity, as reflected by allergic reactions.[2]

These indicators are also used as criteria for performing venom immunotherapy.[3] Venom-specific IgE, once produced in serum after Hymenoptera stings, is expected to disappear time-dependently. However, the disappearance-curve may vary with various factors individually. In order to prevent Hymenoptera hypersensitivity reaction, it is important to identify factors contributing to variation of serum venom-specific IgE level.

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Pest-control operators exterminate many kinds of insects including Hymenoptera. In Japan recently, the numbers of hornets, *Vespa similima. xanthoptera and Vespa analis*, have increased near urban areas, and the incidence of Hymenoptera pest-control has also increased.[4] Thus, pest-control operators have a higher-possibility in being exposed to occupational risk of being stung and experiencing allergic reactions, similar beekeepers and forestry workers. However, to our knowledge, there have been no previous reports of Hymenoptera stings in pest-control operators.

The aim of this study was to evaluate the details of Hymenoptera sting in Japanese pest-control operators and the factors associated with serum venom-specific IgE level which is a diagnostic indicator of Hymenoptera hypersensitivity.

Materials and Methods

Two hundred pest-control operators were asked about episodes of Hymenoptera stings during a routine medical examination, and 118 (59.0%) of these 200 operators were found to have a

history of Hymenoptera stings. Of the 118 operators, 105 granted their informed consent to be study subjects. The study population consisted of 101 male and 4 female subjects, aged from 18 to 65 with a mean age of 37.2 years. They were employees of 14 pest-control companies which belonged to the Pest Control Association of Osaka Prefecture in Japan. Their main job was to exterminate many kinds of vermin, including insects. None of the subjects had received venom immunotherapy.

These 105 subjects were interviewed directly by means of a questionnaire, and blood samples were taken at the same time. The interview and the blood sampling were performed in December 1994.

All of the 105 subjects answered the questionnaire including the following items: (1) the number of past Hymenoptera stings; (2) the time interval from the last sting-incident; (3) identification of the offending insect; (4) location of the sting (s); (5) the number of sting sites; (6) clinical symptoms; (7) individual atopic history; and (8) status as a smoker or nonsmoker. Items (3) to (6) are data related to the last sting-incident only. In the identification of the offending insect, we made the subjects select from 3 subfamilies of Hymenoptera order: Apinae (honeybee), Polistinae (wasp) and Vespinae (yellow jacket and hornet). Clinical symptoms were classified as local reactions (localized pain, swelling, and erythema at the sting site), large local reactions (more extensive local reactions lasting at least 72 hours, without life-threatening signs or symptoms), and systemic reactions (at least one of the following symptoms: generalized urticaria, vomiting, diarrhea, dyspnea, dizziness, feeling of faintness, loss of consciousness, hypotension). Individual atopic history was defined to include atopic dermatitis, urticaria, asthma, or allergic rhinitis.

Serum was obtained from the blood samples. The total serum IgE levels and venom-specific IgE to a yellow jacket (*Vespula sp.*), a wasp (*Polistes sp.*), and a honeybee (*Apis mellifera*) were measured by the CAP system using a commercial kit (CAP RAST FETIA kit, Pharmacia Diagnostics AB. Uppsala, Sweden). In this study, a subject with at least one positive CAP to the 3 kinds of venom was regarded a CAP-positive subject. Of the 3 kinds of venom-specific IgE titer in each subject, the highest one was used in the statistical analysis.

The CAP results for each factor were analyzed by the chi-square test. Spearman's rank analysis was used for correlation between the total serum IgE level and the venom-specific IgE titer. Multiple-regression analysis (using a forward stepwise technique, Fin=Fout=4.0) was performed to evaluate the effect of various factors on the venom-specific IgE titer, with age, gender, questionnaire-items, and the total serum IgE level as the independent variables, and the venom-specific IgE titer as the dependent variable. Before Spearman's rank analysis and multiple-regression analysis, the total and venom-specific IgE values were log transformed. A *P*-value less than 0.05 was considered significant. All the statistical analyses were performed on a personal computer (Macintosh Performa 550, Apple Computer, Inc., Cupertino, USA) using a statistics package (StatView J-4.11, Abacus Concepts, Inc, Berkeley, USA).

Results

The overall features of the Hymenoptera sting-incidents of the 105 subjects are summarized in Table 1. The number of sting-incidents to the time of the interview ranged from 1 to 20, but more than 85% of the subjects have stung 5 times or less; a mean number of the sting-incidents was 3. The time interval from the last sting-incident ranged from 3 months to almost 45 years. Approximately one-half of the subjects was stung more than 10 years before and 11.4% within the last year. Polistinae subfamily (wasp) was identified as the offending insect in 37 subjects (35.2%), followed by Apinae subfamily (honeybee, 23.8%), and Vespinae subfamily (yellow jacket and hornet, 19.0%). Twenty-two percent of the subjects were unable to identify the offending insect. The most frequent sting site was the hand, 61 subjects (58.1%), followed by the head and neck, 38 subjects (36.2%). Eighty-six subjects (81.9%) were stung at only one site on any given occasion. Five subjects (4.8%) had experienced systemic reactions at the most recent attack but none had lost consciousness. Large local reactions were present in 19.0% of the subjects and local reactions in 76.2%.

Table 1 Overall Features of Hymenoptera Sting in 105 Subjects.

	Numbers (%)
Number of past stings	
1	43 (41.0)
2 – 5	49 (46.6)
6 – 9	5 (4.8)
≧10	8 (7.6)
Time interval from the last sting-incident (yrs)*	
<1	12 (11.4)
1 – 2	18 (17.1)
3 – 9	23 (21.9)
10 – 19	28 (26.7)
≧20	24 (22.9)
Kind of offending insect*	
Polistinae (wasp)	37 (35.2)
Apinae (honeybee)	25 (23.8)
Vespinae (yellow jacket and hornet)	20 (19.0)
Unknown	23 (22.0)
Sting location* †	
Hand	61 (58.1)
Head and neck	38 (36.2)
Arm	9 (8.6)
Trunk	7 (6.7)
Leg	6 (5.7)
Number of sting sites*	
1	86 (81.9)
2	10 (9.5)
≧3	9 (8.6)
Clinical symptoms*	
Local	80 (76.2)
Large local	20 (19.0)
Systemic	5 (4.8)

* At the last sting-incident.
†Multiple choice was permitted.

The CAP results for venom-specific IgE are shown in Table 2. Positive CAP to one or more venoms was found in 31.4% (33/105) of the subjects with a history of Hymenoptera stings. Of

Table 2 Serum Levels of Venom-Specific IgE in the 105 Subjects.

	CAP Class*			
	0	1	2	≧3
Yellow jacket	74	11	16	4
Wasp	73	7	16	9
Honeybee	85	3	12	5
Overall CAP †	64	8	20	13

* CAP was graded from class 0-6 and class 2 or more was defined as CAP positive.
†Overall CAP means the highest CAP class of the 3 kinds of venom in each subject.

these 33 positive subjects, 19 (57.6%) had positive CAP to more than one type of venom. In detail, CAP was positive to wasp in 23.8% (25/105), to yellow jacket in 19.0% (20/105), and to honeybee in 16.2% (17/105).

Figure 1 shows the relationship between the frequency of positive CAP and the time interval from the last sting-incident. The frequency significantly decreased with the time interval increased (P<0.001). Positive CAP was found in 60% (18/30) of the subjects stung within the last 3 years and in 20% (15/75) of the remaining subjects. This difference was significant (P<0.001) by chi-square test. Positive CAP with class 3 or more was not observed in the subjects stung more than 10 years before.

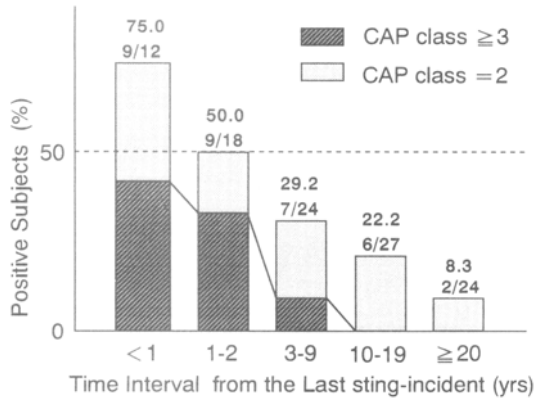

Fig. 1 The relationship between the frequency of positive CAP and the time interval from the jast sting-incident.

Figure 2 shows the relationship between the frequency of CAP-positive subjects and total serum IgE level. The total serum IgE level was under 250IU/ml in 65.7% (69/105) and more than 1000IU/ml in 9.5% (10/105) of the subjects. An increase in the frequency of positive CAP was associated with an increase in the total serum IgE level (P<0.001). Furthermore, a close correlation was found between the venom-specific IgE titer and the total serum IgE level (rs=0.465, P<0.001, Figure 3). The frequency of positive CAP was significantly higher in subjects with total serum IgE level of more than 500IU/ml than in those under 500IU/ml (P<0.001, by chi-square test), and it was 100% in the subjects with total serum IgE level of more than 2000IU/ml.

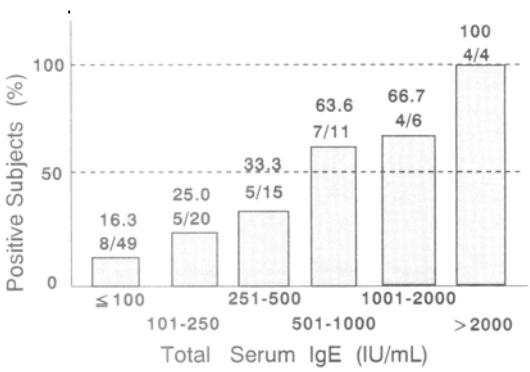

Fig. 2 The relationship of the frequency of positive CAP and the total serum IgE level.

Table 3 shows the association of positive CAP percentage with the various characteristics of the subjects. The frequency of CAP-positive subjects increased significantly in relation to the number of past stings (P<0.05). CAP-positive subjects constituted

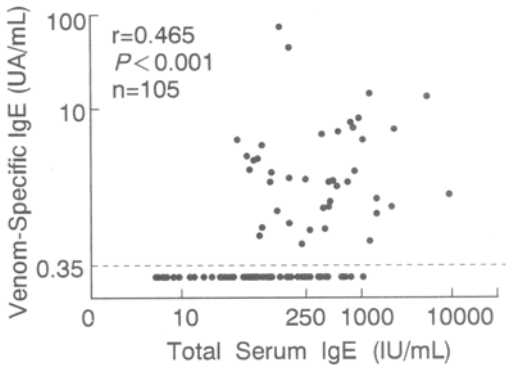

Fig. 3 The relationship between the venom-specific IgE titer and the total serum IgE level.

Table 3 The Correlation between Positive CAP and Other Factors.

	n	Numbers of positives (%)	
Atopic history			
(+)	22	11 (50.0)	P<0.05
(−)	83	22 (26.5)	
Number of past stings			
1	43	10 (23.3)	
2−5	49	14 (28.6)	P<0.05
6−9	5	3 (60.0)	
≧10	8	6 (75.0)	
Clinical symptoms on the latest sting			
Local	80	20 (25.0)	P<0.05
Large local	20	10 (50.0)	
Systemic	5	3 (60.0)	

23.3% (10/43) of the subjects who had suffered from only one sting previously and 75.0% (6/8) of the subjects who had suffered from more than 10 stings. A significant association was observed between the frequency of CAP-positive subjects and the severity of clinical symptoms at the time of the last sting (P<0.05). CAP was positive in 52.0% (13/25) of the allergic subjects with a history of systemic or large local reactions to Hymenoptera stings, and in 25.0% (20/80) of non-allergic subjects with local reactions. CAP-positive subjects constituted one-half of the 22 subjects with a history of atopy and 26.5% (22/83) of the subjects with no history of atopy. This difference was statistically significant (P<0.05). No association was found between the frequency of CAP-positive subjects and the following factors: age, gender, smoking status, type of stinging insect, sting location, and the number of sting sites (data not shown).

Table 4 shows the results of the multiple-regression analysis. Of the 5 factors significantly associated with the frequency of positive CAP, 4 factors were selected (multiple R=0.708, R^2=0.501, adjusted R^2=0.482, P<0.001). Two major factors in particular, the time interval from the last sting-incident and the total serum IgE level, strongly influenced the venom-specific IgE titer. Whereas,

Table 4 Results of the Multiple-Regression Analysis Using a Forward Stepwise Selection for the Independent Variables to Predict the Venom-specific IgE titer.

Independent Variables	β_0	F
Total serum IgE level	0.373	26.625
Time interval from the last sting-incident	0.366	24.264
Number of past stings	0.272	14.032
The most recent clinical symptom	0.174	5.696

Multiple R=0.708, R^2=0.501, adjusted R^2=0.482, p<0.001.

the 2 remaining factors, the number of past stings and the clinical symptoms on the latest sting-incident, did not show such a strong influence as the above 2 factors.

Discussion

Of 200 pest-control operators, a history of Hymenoptera stings was found in 118 (59%) operators. This value was lower than we expected. To compare them with the other occupations, all active beekeepers had experienced Hymenoptera stings[5], and almost all (98.1%) forestry workers had too.[6] Moreover, the estimated number of past stings was less in pest-control operators than in the other 2 occupations. Beekeepers especially were stung often and a previous report showed that active beekeepers suffer from a mean of 10 stings a day during the season.[7] On the other hand, the incidence of systemic reactions to Hymenoptera stings ranges from 14 to 43% in beekeepers[5, 7-10] and 21.4% in forestry workers.[6] These are also more frequent than that in pest-control operators.

Venom-specific IgE, measured by the CAP system, was positive to at least one kind of venom in one-third of the 105 pest-control operators with a history of Hymenoptera stings. Since a history of Hymenoptera stings was found in 59% of 200 pest-control operators, the frequency of positive CAP in overall 200 operators is estimated to be less than 20%. This value is apparently lower than in beekeepers whose frequency ranges from 40 to 70.6%.[8, 10-12] Whereas, although data on estimated number of past stings is scanty in the general population, the incidence of systemic reactions ranges from 0.66 to 3.3%[13-15] and the frequency of positive CAP ranges from 7 to 24%.[16-19] These proportions are similar to those in pest-control operators.

We considered pest control operators to be a high-risk group for Hymenoptera stings same as forestry workers and beekeepers since pest-control operators and beekeepers are constantly in positive contact with Hymenoptera. However, the frequency and number of Hymenoptera stings as well as the frequency of positive CAP in pest-control operators were not very high, which invites the question of why not. In our study, pest-control operators usually used protecting clothes during the extermination of Hymenoptera, and in most cases (almost 80%), they were stung while without their protecting clothes. On the other hand, beekeepers and forestry workers, for the most part, did not use protective clothes.

Venom-specific IgE, once produced by Hymenoptera stings, is expected to disappear time-dependently. In fact, as the time passed from the last sting-incident, the frequency of positive CAP was decreased (Fig. 1). Previous studies also pointed out that the time interval is an important factor for venom-specific IgE level.[11, 20, 21] Since positive CAP was found in only 20% of the subjects stung more than 3 years before, venom-specific IgE is likely to disappear from serum within a few years after the last sting in the majority of CAP negative subjects.

The frequency of positive CAP was significantly higher in subjects with total serum IgE level of more than 500IU/ml than in those under 500IU/ml (Fig. 2), and a significant correlation was found between the venom-specific IgE titer and the total serum IgE level (Fig. 3). In addition, 8 subjects had positive CAP despite having been stung more than 10 years before and 5 of these (62.5%) had total serum IgE level of more than 500IU/ml, and 11 of 12 subjects who was stung within the last 3 years and had negative CAP, had total serum IgE level of under 500IU/ml. These observations indicate that total serum IgE level is also associated with serum venom-specific IgE level.

The number of past stings was also identified as a significantly contributing factor to serum venom-specific IgE level, though the effect was not as strong as the time interval and the total IgE (Table 3 and 4). When the number of past sting increased, venom-specific IgE level was increased. However, Bousquet et al. reported that venom-specific IgE titer was lower when the number of stings increased in beekeepers, and they concluded that less than 25 stings a year induced maximal sensitization, and that more than 200 stings a year was optimal for the desensitization.[10] In pest-control operators, the maximum number of past stings was only 20. As far as a small number of stings, the increase of sting number is considered to contribute to increase venom-specific IgE level.

The clinical symptoms in the last stings are the fourth-strongest factor related to the venom-specific IgE titer, but the influence is very weak compared with the other 3 factors (Table 4). The frequency of positive CAP was significantly higher in subjects with allergic reactions than in others, which is consistent with the previous findings.[6, 9-11] A high venom-specific IgE level in some subjects may be resulted from a strong sensitization and a serious clinical symptom at the last stings.

A significant association was observed between a history of atopy and the frequency of positive CAP (Table 3). Some previous studies found atopic beekeepers have higher venom-specific IgE titer than non-atopic subjects.[7, 9, 16] Total serum IgE level was significantly higher in atopic subjects than in non-atopic subjects (data not shown). The subject with the highest level of total serum IgE (8900IU/ml) was suffering from atopic dermatitis. However, in some atopic subjects, total serum IgE level was not so elevated. Moreover, of the 7 atopic subjects with total serum IgE level of more than 1000IU/ml, 5 (71.4%) had positive CAP, while of the 15 atopic subjects under 500 IU/ml, 6 (40.0%) had. Accordingly, although the total serum IgE level was associated with a history of atopy, it is considered that the presence of venom-specific IgE is surely important irrespective of a history of atopy. In fact, multiple-regression analysis showed that a history of atopy was not significantly related to venom-specific IgE titer.

In conclusion, subjects with elevated total serum IgE level and/or a short time interval from the last sting-incident will have a higher venom-specific IgE titer (positive CAP); and these subjects are considered to be at potentially high risk of Hymenoptera hypersensitivity and thus must take extra care of Hymenoptera stings while at work.

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