

Epidemiologic Investigation of Hornet and Paper Wasp Stings in Forest Workers and Electrical Facility Field Workers in Japan

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ABSTRACT

Background: Forestry and field workers who work outdoors are at high risk for Hymenoptera stings and may develop occupation-related allergies from being stung. However, clinical and immunological surveys of Hymenoptera stings in the occupational setting have rarely been reported. We surveyed the natural history of Hymenoptera stings in Japanese forestry workers (FWs) and electrical facility field workers (EFFWs), and we assessed the utility of measuring specific (s)IgE Ab to Hymenoptera venom.

Methods: Questionnaires on hornet and paper wasp stings were completed by 999 FWs, 354 EFFWs, and 365 office workers as controls between July and November 2009. Sera from these participants were tested for sIgE Ab levels to Hymenoptera venom with a CAP system using a fluoroenzyme immunoassay.

Results: Of the participants who had experienced Hymenoptera stings, 914 (91.5%) were FWs, 293 (82.8%) were EFFWs, and 295 (80.8%) were controls. Of the participants who had experienced systemic reactions, 210 (21.0%) were FWs, 51 (14.4%) were EFFWs, and 39 (10.7%) were controls. sIgE Ab in response to hornet and wasp venom was positive ($\geq$ class 2) in 42.4% and 41.4% of FWs, 30.1% and 31.4% of EFFWs, and 15.1% and 18.1% of controls, respectively. The likelihood of being sIgE-positive to wasp and hornet venom was significantly higher in FWs and EFFWs than in controls ($P < 0.05$).

Conclusions: 21% of FWs and 14% of EFFWs had experienced systemic reactions to Hymenoptera stings with a higher frequency compared with office workers in the same area. 40% of FWs and 30% of EFFWs had sera that were sIgE positive to Hymenoptera venom.

KEY WORDS

forestry and field workers, hornet stings, Hymenoptera allergy, paper wasp stings, venom-specific IgE

ABBREVIATIONS

SR, systemic reaction; OR, odds ratio; RAST, radioallergosorbent test; CAP, immunoCAP; FEIA, fluoroenzyme immunoassay; FWs, forestry workers; EFFWs, electrical facility field workers; OW, office workers; sIgE, specific IgE; Ab, antibody.

INTRODUCTION

The number of deaths attributed to Hymenoptera

stings is about 40 per year in the United States^{1,2} and about 16 to 38 per year in France.³ In addition, fatalities following insect stings are rare and occur in 0.03-

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0.48 per 100000 inhabitants per year.^{4,6} These data are largely from studies carried out in the United States and Europe. Furthermore, Pumphery^{7,8} reported that between 1992 and 2001 in the United Kingdom, 47 out of 214 deaths, due to anaphylaxis, were caused by bee or wasp stings and the average age of death was 50 years.⁸ On the other hand, in Japan approximately 20 people die annually of anaphylaxis caused by Hymenoptera stings.⁹ Not only bee-keeper but also forestry and field workers who work outdoors are at especially high risk for these stings, and may develop occupational-related allergies from being stung. In the bee keepers and their family members, the sensitization rate to bee venom is 30-60%.⁶ The prevalence of local reactions is 9-31%, and the prevalence of systemic reactions is 14-32%. Venom allergy is an important cause of anaphylaxis accounting for about one quarter of cases where the cause was determined in adults.⁷

The clinical and immunological surveys of Hymenoptera stings in the occupational setting, especially forestry and field workers, have rarely been reported. Here we recently conducted a large epidemiological study to survey the natural history of Hymenoptera stings in Japanese forestry and field workers, and in office workers as controls.

METHODS

PARTICIPANTS

A total of 1,718 participants agreed to take part in this study (Table 1). Forestry workers (FWs) were staff members of a private forest owner's cooperative in Tochigi and Fukushima prefectures, Japan and electrical facility field workers (EFFWs) were employed by Tokyo Electric Power, Kandenko, Tokyo and Tochidenko, Tochigi, Japan. The main work of FWs is forestation, which includes weeding, planting, and felling of trees, and these workers are frequently exposed to Hymenoptera stings. EFFWs also usually work outdoors and are at a high risk of Hymenoptera stings. In comparison, office workers in the same area have a low risk for exposure to Hymenoptera stings and were recruited as controls in this study. All participants completed questionnaires and underwent peripheral blood tests between July and November 2009.

This study was approved by the Dokkyo Medical University Research Ethics Committee, and written informed consent was obtained from each participant prior to study enrollment.

QUESTIONNAIRE

A questionnaire on the following items was administered by an allergist: age; sex; history of Hymenoptera stings; and history of systemic reaction (SR), including severity. The severity of anaphylactic reactions was classified according to the method of Mueller¹⁰: grade 0, no systemic reaction; 1, skin symptoms

(generalized urticaria, itching, or erythema) or anxiety; 2, gastrointestinal symptoms (stomach pain, nausea, or vomiting) or angioedema; 3, respiratory symptoms (dyspnea, difficulty swallowing, hoarseness, or stridor); and 4, cardiovascular symptoms (hypotension defined as a decrease of 15 mm Hg or more in mean arterial pressure, requiring immediate intervention, with or without cyanosis, collapse, arrhythmias, or angina pectoris). The symptoms of each participant were classified according to the most severe symptoms that he or she had experienced.

To analyze the relationship between frequency of Hymenoptera stings and severity of systemic reaction, the participants were classified according to the number of Hymenoptera stings they had experienced: few (1-5), intermediate (6-10), and many (≥ 11). Systemic reaction was classified as mild (grades 1-3) or severe (grade 4).

BLOOD TESTING

A 15-mL peripheral blood sample was drawn from each participant. Serum was extracted and stored at -80°C until used for analysis. We measured total serum IgE antibody (Ab) and sIgE Ab to Hymenoptera venom in FWs, EFFWs, and controls. The measurement of total IgE Ab (>250.0 IU/mL) and sIgE Ab to wasp and hornet venom was determined by Mitsubishi Chemical, SRL, Tokyo, Japan. Detection of sIgE Ab by the CAP-fluoroenzyme immunoassay (FEIA) system is expressible in quantitative units (kIU/L) and also in the traditional spectrum of seven semi-quantitative classes ranging from class 0 (<0.35 kIU/L) to class 6 (>10 kIU/L). sIgE Ab-positive results were defined as those $\geq$ class 2, considering the effects of cross-reactive carbohydrate determinants.¹¹

STATISTICAL ANALYSIS

Data are presented as mean $\pm$ standard deviation of the mean. Student *t* tests were used to assess the significance of difference between the groups. The χ^2 test was used to assess differences in bivariate analysis and revised with analysis of variance with Bonferroni's test. The χ^2 test was also used to test for independence and odds ratio (OR). *P* values of less than 0.05 were considered to indicate statistical significance. Statistical analyses were performed with JMP software (Version 7.0 for MAC, SAS Institute, Cary, NC, USA).

RESULTS

ANALYSIS OF QUESTIONNAIRE DATA

Table 1 summarizes the characteristics of FWs and EFFWs in this study, based on the questionnaire data provided. The number of participants (mean age) in the FWs, EFFWs, and controls were 999 (51 ± 14.0 years), 354 (42 ± 15.1 years), and 365 (50 ± 11.7 years), respectively. In the FWs and EFFWs, all participants were male; in the controls, 231 were male

Table 1 Subject characteristics (*n* = 1718)

	† FWs	‡ EFFWs	§ Controls
No. of participants	999	354	365
Age, y mean ± SD (range)	51 ± 14.0 (18-82)	42 ± 15.1 (18-77)	50 ± 11.7 (19-78)
Male, <i>n</i> (%)	999 (100)	354 (100)	231 (63.3)
Female, <i>n</i> (%)	0 (0)	0 (0)	134 (36.7)
History of stings, <i>n</i> (%)	914 (91.5)	293 (82.8)	295 (80.8)
No. of stings			
Few (1-5)	451 (45.1)	186 (52.5)	256 (70.1)
Intermediate (6-10)	258 (25.8)	55 (15.5)	21 (5.8)
Many (≥11)	103 (10.3)	22 (6.2)	5 (1.4)
Unknown	102 (10.2)	30 (8.5)	13 (3.6)
Symptoms, <i>n</i> (%)			
Local reaction	621 (62.2)	228 (64.4)	222 (60.8)
LLR	198 (19.8)	44 (12.4)	50 (13.7)
SR Total	210 (21.0)	51 (14.4)	39 (10.7)
Grade I	129 (12.9)	29 (8.2)	26 (7.1)
II	17 (1.7)	5 (1.4)	3 (0.8)
III	19 (1.9)	5 (1.4)	0 (0.0)
IV	45 (4.5)	12 (3.4)	10 (2.7)
Total IgE (IU/ml) (mean ± SD)	300.8 ± 126.0	307.4 ± 192.3	205.7 ± 124.5

† FWs, forestry workers; ‡ EFFWs, electrical facility field workers; § Controls consisted of office workers.

SD, standard deviation of the mean; LLR, large local reaction; SR, systemic reaction.

Table 2 CAP results of wasp and hornet venom among three occupational subgroups

CAP (class)	Wasp			Hornet		
	† FWs (%)	‡ EFFWs (%)	§ Controls (%)	† FWs (%)	‡ EFFWs (%)	§ Controls (%)
0	467 (46.7)	212 (59.9)	264 (72.3)	448 (44.8)	208 (58.8)	279 (76.4)
1	118 (11.8)	31 (8.8)	35 (9.6)	127 (12.7)	38 (10.7)	31 (8.5)
2	260 (26.0)	67 (18.9)	48 (13.2)	272 (27.2)	70 (19.8)	43 (11.8)
3	128 (12.8)	36 (10.2)	16 (4.4)	125 (12.5)	26 (7.3)	10 (2.7)
4	22 (2.2)	6 (1.7)	0 (0.0)	24 (2.4)	4 (1.1)	1 (0.3)
5	3 (0.3)	2 (0.6)	1 (0.3)	3 (0.3)	3 (0.8)	1 (0.3)
6	1 (0.1)	0 (0.0)	1 (0.3)	0 (0.0)	5 (1.4)	0 (0.0)
≥class 2 (%)	414 (41.4)	111 (31.4)	66 (18.1)	424 (42.4)	108 (30.1)	55 (15.1)

† FWs, forestry workers; ‡ EFFWs, electrical facility field workers; § Controls consisted of office workers.

and 134 were female. The number of participants who had experienced Hymenoptera stings was 914 (91.5%) in the FWs, 293 (82.8%) in the EFFWs, and 295 (80.8%) in the controls. The number of participants who had experienced systemic reactions was 210 (21.0%) in the FWs, 51 (14.4%) in the EFFWs, and 39 (10.7%) in the controls, respectively. These results indicate that the incidence of systemic reactions to Hymenoptera stings is high, especially in FWs. The mean IgE Ab level was 300.8 ± 126.0 IU/ml in FWs, 307.4 ± 192.3 IU/ml in EFFWs, and 205.7 ± 124.5 IU/ml in controls.

SERUM sIgE Ab TO HORNET AND WASP VENOM

We measured serum sIgE Ab (Table 2) to hornet and wasp venom in FWs, EFFWs, and controls. sIgE Ab to wasp and hornet venom was ≥class 2 in 414 (41.4%) and 424 (42.4%) FWs, 111 (31.4%) and 108 (30.1%) in EFFWs, and 66 (18.1%) and 55 (15.1%) in controls, respectively. The likelihood of being sIgE Ab positive to wasp and hornet venom was significantly higher in FWs and EFFWs than in controls (*P* < 0.05; Table 3). The odd ratios (ORs) for these positive tests, relative to controls, were as follows: in FWs, wasp OR 4.2 (95% confidence interval [CI], 3.0-5.7) and hornet OR 4.0 (95% CI, 2.9-5.5); in EFFWs, wasp OR 2.3 (95% CI, 1.6-3.3) and hornet OR 2.6 (95% CI, 1.8-3.7). The sIgE

Table 3 Relationship of positive CAP results to wasp and hornet venom among three occupational subgroups

	sIgE positive number (%)	OR	95% CI	P value
<i>Wasp</i>				
§ Controls	66 (18.1)	-	-	-
† FWs	414 (41.4)	4.2	3.0-5.7	<0.05
‡ EFFWs	111 (31.4)	2.3	1.6-3.3	<0.05
<i>Hornet</i>				
§ Controls	55 (15.1)	-	-	-
† FWs	424 (42.4)	4.0	2.9-5.5	<0.05
‡ EFFWs	108 (30.1)	2.6	1.8-3.7	<0.05

† FWs, forestry workers; ‡ EFFWs, electrical facility field workers;

§ Controls consisted of office workers.

OR, odds ratio; CI, confidence interval. *P* values apply to comparisons with the controls.

Ab positive results to both wasp and hornet were significantly higher in FWs and EFFWs than in controls ($P < 0.05$).

RELATIONSHIP BETWEEN FREQUENCY OF HYMENOPTERA STINGS AND SEVERITY OF SYSTEMIC REACTION

Finally, we examined the relationship between frequency of Hymenoptera stings and severity of systemic reaction in 275 subjects, excluding 25 subjects with an unknown number of Hymenoptera stings (Table 4). In 1502 subjects with a past history of Hymenoptera stings, the number of the stings correlated significantly between the controls and FWs ($P < 0.01$), between FWs and EFFWs ($P < 0.05$), and between the EFFWs and controls ($P < 0.05$), respectively, according to the results of the Chi-squared test (Table 1). On the other hand, in 275 subjects who had experienced systemic reactions to the stings, the number of Hymenoptera stings did not correlate significantly with the presence (data not shown) or severity of systemic reactions (Table 4). Namely, the number of Hymenoptera stings was similar in the subjects who had experienced systemic reactions, irrespective of the occupations.

DISCUSSION

Allergic reactions to insect stings are reported by approximately 0.4% of the population in the United States¹² and by 1.2% of adults in France.¹³ Recent cross-sectional surveys in the United States,¹⁴ Greece,¹⁵ Germany,¹⁶ and Sweden¹⁷ have shown a 1-3% prevalence of systemic reactions and a 9-32% prevalence of sensitization to insect venoms, as measured by a skin test or immunoassay. In another study, Hymenoptera stings related to occupation occurred in 98.1% of 323 Japanese FWs surveyed.¹⁸ Among these FWs, 21.8% had hypersensitivity to Hymenop-

Table 4 Relationship between the number of past Hymenoptera stings and severity of systemic reaction in 275 subjects, excluding 25 with an unknown number of Hymenoptera stings

	Systemic reaction [†]		
	None (%)	Mild (%)	Severe (%)
No. of stings			
Few (1-5)	54 (19.6)	31 (11.3)	10 (3.6)
Intermediate (6-10)	41 (14.9)	19 (6.9)	6 (2.2)
Many (≥11)	76 (27.6)	33 (12.0)	5 (1.8)

[†] Systemic reaction was classified as mild (grade 1-3) or severe (grade 4), according to the method of Mueller.¹⁰

tera stings, defined by a history of systemic urticaria and/or dyspnea after a sting.¹⁸ Similarly, the present survey revealed a history of Hymenoptera stings in over 90% of the 999 FWs and systemic reactions in 23.0% of 54 FWs. The risk of a systemic reaction to Hymenoptera stings was higher in FWs than in EFFWs and controls. These results indicate that FWs are more likely to be exposed to Hymenoptera stings than EFFWs and office workers.

Detectable sIgE Ab to venom plays an important role in the diagnosis of acquired Hymenoptera hypersensitivity.¹⁹⁻²² Several researchers have reported that the prevalence of positive skin tests or positive tests for sIgE Ab to Hymenoptera venom is 15-25% in the general population.²³ The levels of hornet and wasp sIgE Ab in these participants correlate significantly with each other. These findings suggest cross-reactivity to venom antigens from hornet and wasp. In addition, double positivity to wasp and bee venom occurs in about 30% of patients clinically allergic to only one insect²⁴ and is often due to cross-reactivity of venom-specific IgE Ab with specific carbohydrate ligands.²⁵ We also demonstrated that the levels of hornet and wasp sIgE Ab in these participants correlated significantly with each other ($R = 0.82$, $P < 0.001$).

Shimizu *et al.*¹⁸ reported that a positive radioallergosorbent test (RAST) (≥class 1) to hornet and wasp venom occurred in 26.3 and 22.3% of 323 FWs, respectively. In our study, approximately 40% of FWs, 30% of EFFWs, and 15% of office workers were positive for sIgE Ab (≥class 2) to hornet and/or wasp venom. The prevalence of sIgE Ab-positive tests in FWs was greater than in both other groups. Our results revealed a notably higher prevalence of allergic constitution compared with the study by Shimizu *et al.*. These differences may be due to a higher sensitivity in the assay used in the present study—the CAP-FEIA system involves a porous sponge solid phase, while the RAST system involves a paper disc.²⁶

The risk of systemic reactions in the general population is increased by 58% if preceded by a sting

within 2 months, even if the first sting is well tolerated by a positive sIgE Ab to Hymenoptera venom.²⁷ The estimated risk of a systemic reaction is 5-15%²⁸ following a previous large local reaction and 40-60%²⁹ after a systemic reaction. In addition, sIgE Ab levels decline over several years if a person does not experience a subsequent Hymenoptera sting.³⁰ Persons who have experienced frequent Hymenoptera stings have increased levels of sIgE Ab to Hymenoptera venom and may experience frequent systemic reactions to additional Hymenoptera stings in a comparatively short timeframe. These findings suggest a correlation between the high frequency of past systemic reactions and positive sIgE to Hymenoptera venom.

In terms of the relationship between the number of past Hymenoptera stings and the severity of systemic reactions, Pastorello *et al.*³¹ reported that the practice of bee-keeping induces a relatively high incidence of allergic reactions, but with a trend to spontaneous improvement of symptoms and a low incidence of severe reactions. These results suggest that natural frequent bee stings are similar to venom immunotherapy. On the other hand, in our study, the number of stings did not correlate with the severity of systemic reactions. This may be the case because FWs and EFFWs are stung at irregular and/or indeterminate intervals, that is, in a manner that does not resemble venom immunotherapy.

In conclusion, 21% of FWs and 14% of EFFWs had experienced systemic reactions to Hymenoptera stings with a higher frequency compared with office workers in the same area. 40% of FWs and 30% of EFFWs had sera that were sIgE positive to Hymenoptera venom.

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