
Risk factors for systemic reactions to bee venom in British beekeepers

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Background: There is a high incidence of systemic reactions (SRs) to bee stings in beekeepers, but the factors predisposing individuals to such responses are not well understood.

Objectives: To identify factors that predispose British beekeepers to SRs and to investigate how beekeepers access specialist services after SRs to bee venom.

Methods: A link to an online survey was published in the bimonthly magazine and on the Web site of the British Beekeepers Association. The demographic results are presented using descriptive analysis, and a logistic regression model was used to determine risk factors for SRs.

Results: There were 852 responses to the questionnaire of which 63% were from male beekeepers; the most common age range was 51 to 60 years. Twenty-eight percent of all responders had experienced a large local reaction and 21% had experienced a SR. Factors that predisposed beekeepers to SRs included female sex, having a family member with bee venom allergy, more than 2 years of beekeeping before a SR, and premedication with an antihistamine before attending the hives. A total of 44% of beekeepers with SRs attended the emergency department because of their symptoms, 16.6% were reviewed by an allergy specialist, and only 18% carried an adrenaline autoinjector.

Conclusions: Logistic regression analysis identified a number of novel factors to be associated with the development of SRs. Rates of attendance at the emergency department, allergy specialist review, and carriage of adrenaline were low, highlighting a need for education in the beekeeping community and among health care professionals.

Ann Allergy Asthma Immunol. 2011;106:159–163.

INTRODUCTION

Beekeepers are heavily exposed to honeybee (*Apis mellifera*) stings, and previous studies have suggested that they are at a higher risk of developing bee sting allergy than the general population. Bee venom allergy ranges in severity from large local reactions to a wide range of systemic reactions (SRs) and fatal anaphylaxis.¹ Previous European studies have shown considerable variation in the prevalence rates and risk factors predisposing individuals to SRs,^{2–6} which have been attributed to climate, geographical location, data collection technique, definition of allergic reaction, and degree of exposure. Local information would contribute to our understanding of the natural course of bee venom allergy in the British population, allowing planning of services and risk stratification of beekeepers with bee venom allergy.

The main objective of this survey was to determine the factors associated with allergic SRs to bee stings in British beekeepers. This study also examined how beekeepers ac-

cessed specialist services for further assessment and management of bee venom allergy.

METHODS

Study Participants

The British Beekeepers Association (BBKA) is a national body that encompasses 62 affiliated regional associations with a combined membership of 12,000 beekeepers. All members receive a bimonthly newsletter either by electronic mail or post. The link to the online open survey was advertised to all members through the magazine and on the association Web site. The survey was constructed and data collected using surveymonkey.com software (SurveyMonkey, Menlo Park, California). The local ethics committee was approached for guidance, and no formal application was required.

Study Questionnaire

A questionnaire was devised to investigate risk factors for bee venom allergy and the use of National Health Service allergy service. The information requested included demographic data, resident county, history of venom allergy in family members, number of years beekeeping, stings per year, time from start of beekeeping to first reaction, bee species kept, prophylactic use of antihistamine, concurrent atopic disease, comorbid cardiac and/or respiratory disease, severity of sting reaction (using a modified Muller grading system; for description see question 11 of eQuestionnaire), review by an

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Disclosures: Authors have nothing to disclose.

Received for publication July 19, 2010; Received in revised form October 14, 2010; Accepted for publication November 2, 2010.

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doi:10.1016/j.anai.2010.11.005

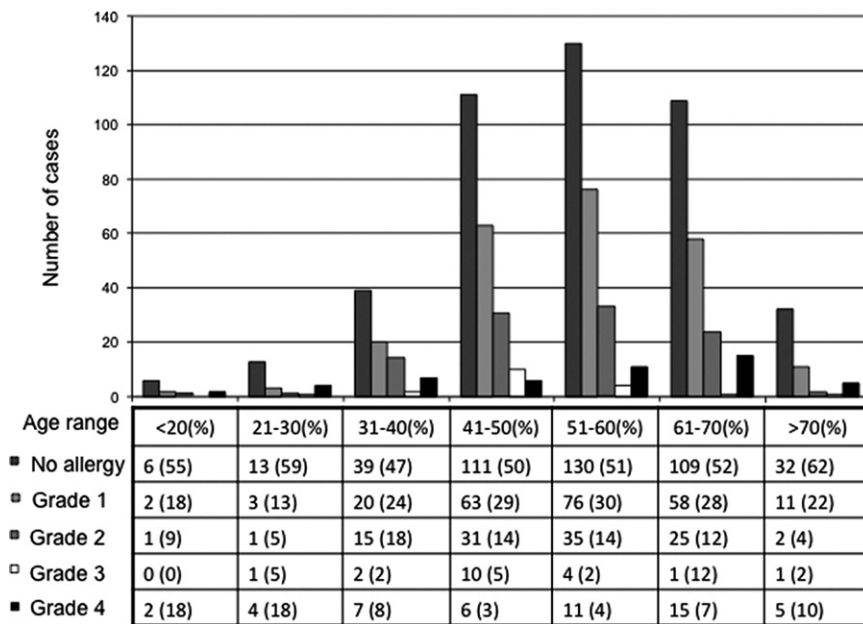


Figure 1. Incidence and grade of venom allergy in each of the age categories. There were a total of 852 responses. Percentage of age range group shown in brackets and rounded up to nearest whole number.

allergy specialist after the SR, prescription of an adrenaline autoinjector, and venom immunotherapy (VIT). Data on efficacy were collated from patients who were prescribed VIT.

Statistical Analysis

Simple descriptive statistics were used to describe the population. A logistic regression model was developed to determine the odds of having had an SR in one category compared with another. Data are expressed as odds ratios with 95% confidence intervals. Access to service data was analyzed using the Pearson χ^2 test with 2-tailed significance. The county area where hives were kept was retrospectively reanalyzed into geographic regions. SPSS statistical software, version 15.0 (SPSS Inc, Chicago, Illinois), was used for all data analyses. $P < .05$ was considered significant.

RESULTS

Demographics

There were 852 complete responses to the questionnaire. There were 816 complete data responses, and of these there were 545 male respondents and 271 female. The most common age range was 51 to 60 years.

History of SRs

Of the 852 respondents, 412 (48%) had experienced an allergic reaction to a bee sting: grade 1, 233 (27%); grade 2, 111 (13%); grade 3, 19 (2.3%); and grade 4, 49 (6%) (Fig 1). A total of 127 of beekeepers (15%) had a close family member who had bee venom allergy.

Risk Factors for Increasing Severity of Venom Allergic Reaction

Risk factors for a SR included having a family member with a venom allergy, female sex, more than 2 years of beekeeping, more than 2 years of beekeeping before first reaction, and premedication with antihistamine before attending the hives (Table 1). A sting rate between 75 and 150 stings per year, eczema, and asthma showed significant associations ($P \leq .01$), but with odds ratios less than 1, the associations were inverse and indicate possibly favorable relationships when any of these conditions coexist with history of SRs. Keeping a specific subspecies of bee did not predispose beekeepers to an SR (data not shown).

Medical Services Accessed

One hundred of the 412 beekeepers (24%) who had experienced a reaction to bee venom sought treatment at the emergency department, and 66 (16%) of the 412 beekeepers had seen a hospital-based specialist as an outpatient. Ninety-five of the 412 beekeepers (23%) had an adrenaline autoinjector prescribed, but of these only 75 carried the adrenaline to the hives and only 35 carried the adrenaline at all times. Seventy-nine (44%) of the 179 beekeepers who had reported SRs sought treatment at the emergency department after a bee sting. One hundred beekeepers who had experienced a grade 2 (70), 3 (15), or 4 (15) reaction did not seek medical attention. There were no statistical differences in emergency department attendance (Pearson χ^2 test, $P = .51$), review by hospital specialist ($P = .76$), or prescription of adrenaline autoinjector ($P = .79$) among the regions (data not shown).

Table 1. Risk Factors for a Systemic Reaction After Bee Stings^a

Risk factor	OR (95% CI)	P value
Age, y		
<20	2.048 (0.443–9.470)	.36
21–30	1.792 (0.550–5.841)	.33
31–40	1.962 (0.825–4.670)	.13
41–50	1.345 (0.611–2.957)	.46
51–60	1.200 (0.549–2.625)	.65
61–70	1.232 (0.556–2.732)	.68
Female sex	1.905 (1.353–2.681)	<.001
Family member with allergy	2.237 (1.482–3.377)	<.001
Smoking status		
Current	1.775 (0.883–3.784)	.14
Ex	0.915 (0.624–1.340)	.65
Stings per year		
0–25	0.468 (0.151–1.453)	.19
25–75	0.348 (0.103–1.175)	.09
75–150	0.13 (0.026–0.657)	.01
150–200	0.686 (0.119–3.963)	.67
Time beekeeping before first reaction, y		
2–5	5.674 (3.261–9.876)	<.001
5–10	14.159 (4.746–42.245)	<.001
>10	7.387 (3.022–18.062)	<.001
Total time beekeeping, y		
2–5	3.405 (1.890–6.134)	<.001
5–10	3.591 (1.872–6.890)	<.001
>10	3.716 (2.075–6.656)	<.001
Eczema	0.416 (0.211–0.821)	.01
Asthma	0.470 (0.244–0.903)	.02
Hay fever	0.925 (0.623–1.375)	.70
Antihistamine before hives	6.239 (3.521–11.057)	<.001

Abbreviations: CI, confidence interval; OR, odds ratio.

^a Risk factors for a systemic reaction generated using a logistic regression model, which determined whether different categories within a variable predisposed a beekeeper to a systemic reaction. The reference groups for this table are older than 70 years, never smoked, more than 200 stings per year, less than 2 years of beekeeping before a first reaction, and less than 2 years of total beekeeping.

Venom Immunotherapy

Thirty-two beekeepers have undergone VIT. There were 2 withdrawals because of severe reactions to the injections. Twenty patients had experienced a sting either during or after VIT, which was associated with a statistically lower-

grade reaction (mean difference, 1.4 grades; Wilcoxon signed rank test, $P < .006$). Four of 20 patients (20%) experienced a systemic allergic reaction after cessation of VIT. Preexisting heart or lung disease could not predict failure of VIT (data not shown).

DISCUSSION

This survey represents one of the largest studies of bee venom allergy in beekeepers and the first in the United Kingdom. SRs were reported in 21% of respondents, and a further 28% reported local reactions. This study identified that a number of factors, including having a family member with bee venom allergy, female sex, more than 2 years of beekeeping, and premedication with antihistamines, were associated with development of SRs. Attendance at emergency department and subsequent allergy specialist review was surprisingly low, which is a likely explanation for the low proportion of beekeepers who received VIT after an SR.

Our survey identified a number of previously unidentified factors associated with a history of SRs, including having a family member with a venom allergy, female sex, more than 2 years of beekeeping, more than 2 years of beekeeping before first reaction, and premedication with an antihistamine before attending the hives. In concordance with other studies, a sting rate of 75 to 150 stings per year was also associated with a lower SR rate. In contrast to a previous study that identified an atopic predisposition as being a risk factor for SRs,³ our data showed that in eczema and asthma the associations were inverse and indicate possibly favorable relationships when these conditions coexist with a history of SRs. An atopic constitution does not predispose the general population to venom allergy⁷; however, there has been one previous study suggesting a link in beekeepers.

Beekeepers, their family members, and their neighbors are in a high-risk group, most likely because of increased exposure and a higher sting rate than the general population.³ To our knowledge, this is the first report to highlight that having a relation with bee venom allergy was associated with higher odds of developing an SR. A limitation of our data is that further details, regarding the family pedigree, were not obtained in the questionnaire. Identification of the status of the family member with bee venom allergy would establish whether this is linked to a hereditary

Table 2. Beekeeper Epidemiologic Studies

Source	Country	No. studied	No. (%) of local reaction	No. (%) of systemic reactions
Current study, 2009	Britain	826	235 (28)	169 (20)
Munstedt et al, ⁵ 2008	Germany	1053	797 (76)	46 (4)
Celikel et al, ¹⁹ 2006	Turkey	494	NA	29 (6.5)
Garcia-Robaina et al, ⁶ 1997	Canary Island	246	75 (31)	53 (21)
Annala et al, ²⁰ 1996	Finland	191	50 (26)	73 (38)
Bousquet et al, ²¹ 1994	France	200	24 (12)	28 (14)
Pastorello et al, ²² 1988	Italy	222	31 (14)	21 (9.0)

Abbreviation: NA, not available.

component or whether the higher odds of SR are related to more frequent and intense contact. A more objective evaluation of the allergic reactions of the index case and the family member will help to clarify this potential risk factor because family perceptions of allergy may potentially bias the response. Female sex was associated with a higher odds of an SR, which is in contrast to the German study,⁵ which showed no sex difference. Sex studies usually center around the role of sex hormones, and recently androgen receptors have been demonstrated on human mast cells⁸ and estrogens have been shown to enhance IgE-dependent mast cell activation.⁹ Female sex is a risk factor for other immediate-type hypersensitivity disorders,¹⁰ and this study suggests that further investigation in bee venom allergy is warranted.

Premedication with antihistamines before going to the hives was identified as a novel association for an SR, and this warrants further investigation because it has implications for management. It is beyond the scope of this study to determine whether beekeepers who had previously experienced reactions took a prophylactic antihistamine or whether premedication predisposed individuals to SRs. There are several reports that antihistamine pretreatment before VIT injections reduces the frequency of large local reactions and mild SRs^{11,12} but not anaphylactic reactions.^{13,14}

Only 25% of beekeepers who experienced an SR attended the emergency department. It is unknown from this survey how the reaction was managed or why in some cases emergency medical services were not sought. Only 66% of beekeepers who attended the emergency department with an SR were reviewed by an allergy specialist for further management. Referral to allergy services allows assessment for VIT, which is the only effective treatment for the prevention of anaphylaxis in bee venom allergy. In this cohort, VIT significantly reduced the severity of subsequent SRs to a bee sting but with a 20% failure rate consistent with previous reports.^{15,16}

The failure of beekeepers to attend the emergency department with SRs reveals a need for education in this high-risk group. Although adrenaline autoinjectors were prescribed for 95 patients (23% of all beekeepers who had venom allergy), only 75 carried them to the hives and 35 carried them at all times. A UK survey of fatal anaphylaxis cases has shown that collapse and shock occur within 15 minutes of the sting, highlighting the importance of carrying adrenaline at the hives, early administration in anaphylaxis, and prompt attendance at medical services.¹⁷

There are other limitations to this study. This was an open survey (ie, beekeepers were not directly contacted); therefore, the precise response rate is uncertain. This survey was completed by members of the BBKA with access to the Internet, and restriction to this facility may have influenced results. Also, the data on the number of beekeepers receiving bi-monthly newsletters electronically are not known. Although a number of members of the BBKA continued beekeeping despite a history of venom allergy, it is likely that a proportion of individuals withdrew from beekeeping and the BBKA after anaphylaxis, and accessing these patients would be

difficult. On the other hand, patients who have experienced an SR may have been more likely to complete the questionnaire. Overestimation has been previously demonstrated in food allergy questionnaire-based studies.¹⁸ The overall response rate to the questionnaire is similar to published studies in this field.⁵

The true percentage of beekeepers who experience SRs after bee sting cannot be ascertained from this survey, and ascertainment was not a primary objective. This study found that 21% of people who were stung had a history of SRs, which falls within the range described in previous studies (Table 2). A further limitation of this study is that the history of bee venom allergy is self-reported and self-reported reactions are susceptible to bias. This questionnaire-based study was not able to ascertain supporting immunologic or clinical data for anaphylaxis, and this could usefully be addressed in future studies.

In conclusion, this survey has highlighted that female sex, having a family member with bee venom allergy, more than 2 years of beekeeping before an SR, and premedication with an antihistamine before visiting hives were associated with a history of SRs in British beekeepers. The limitations of this study suggest the need for further investigation to corroborate these findings. It is concerning that a significant proportion of beekeepers who experienced SRs did not obtain emergency medical services or advice from a specialist. This highlights a need for education in both beekeepers and health care professionals.

ACKNOWLEDGMENT

We thank the BBKA and its members for helping to disseminate and complete the questionnaire. We are grateful to Professor Stephen Durham for reviewing the manuscript.

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