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The Hymenoptera venom study I, 1979-1982: Demographics and history-sting data

Richard F. Lockey, MD, Paul C. Turkeltaub, MD, Irene A. Baird-Warren, Christine A. Olive, Emory S. Olive, Brett C. Peppe, and Samuel C. Bukantz, MD Tampa, Fla., and Bethesda, Md.

The Hymenoptera venom study, a study based on case histories, skin test results and adverse reactions, immunotherapy and adverse reactions, and treatment efficacy, for 3236 Hymenoptera-allergic subjects, was begun in 1979 after the Food and Drug Administration approval of Hymenoptera venoms. Eighty-four Fellows and Members of the American Academy of Allergy and Immunology participated in the study. All subjects had a history of an adverse reaction to one or more Hymenoptera insects. The mean age was 30½ years (range 1 to 83 years). Male subjects accounted for 61.5% and female subjects, 38.5%; 3.1% were beekeepers and 32.3% were atopic. Demographic data were similar for subgroups. There was an average of 2.7 history stings per subject. At least one systemic reaction (SR) was reported by 2866 subjects (89%); 2219 (69%) experienced an SR after their most recent sting before entry into the study, and 70% had experienced only a single SR. Moderate to severe SRs were equally likely after stings of yellow jacket, white-faced hornet, and yellow hornet (65%), honeybee (67%), or wasp (70%), although historical SRs were reported more often after stings of yellow jacket, white-faced hornet, or yellow hornet (30%) than after honeybee (19%) or wasp (14%) stings. No association was noted between the number of stings per episode and severity of the SR. Fifty-one percent of SRs were reported as occurring within 10 minutes of sting; however, the onset of a moderate to severe SR sometimes occurred at 301 or more minutes after a sting episode. Of 2219 subjects with an SR after their most recent sting before entry into the study, 68% received epinephrine for treatment. (J ALLERGY CLIN IMMUNOL 1988;82:370-81.)

From the Division of Allergy and Immunology, Department of Medicine, University of South Florida College of Medicine, and James A. Haley Veterans Administration Hospital, Tampa, Fla., and Laboratory of Allergenic Products, Office of Biologics Research and Review, Food and Drug Administration, Bethesda, Md.

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Reprint requests: Richard F. Lockey, MD, Director, Division of Allergy and Immunology, University of South Florida College of Medicine, c/o VA Hospital (VAR 111D), 13000 Bruce B. Downs Blvd., Tampa, FL 33612.

When venom extracts became commercially available late in 1979, an HVS was initiated by questionnaire by the American Academy of Allergy and Immunology Committee on Insects. The study was based on the case histories and VST results of 3236 subjects who had reacted adversely, either with an SR or LR, to stings by Hymenoptera insects. Information was submitted by 84 Fellows and Members of the Academy, and follow-up data were available for most subjects.

The goals of the Therapeutic Safety and Efficacy Protocol were (1) to ascertain the frequency and severity of in-field SSR (with signs and/or symptoms as listed below) in subjects with a history of previously

Abbreviations used:

AAAI:	American Academy of Allergy and Immunology
HVS:	Hymenoptera venom study
LLR:	Large local reaction
LR:	Local reaction
MRSPEs:	Most recent sting prior to entry into the study
SR:	Systemic reaction
SRI:	Systemic reaction index
SSR:	Sting systemic reaction
VST:	Venom skin test
WBE:	Whole body extract

experienced SSR, who were VST positive when they were first tested, and were administered venom immunotherapy and were subsequently resting in the field, or were administered venom immunotherapy, had immunotherapy stopped either before or after achievement of maintenance level, and were subsequently resting in the field, and (2) to ascertain the frequency and severity of adverse reactions (anticipated and unanticipated) occurring during skin testing and/or venom immunotherapy.

The goals of the Diagnostic Efficacy Protocol were (1) to predict whether a subject is more likely to have an SSR if that subject had previously experienced an SSR, were VST negative, and were resting in the field, or if a subject were VST positive but had either refused venom therapy or it had been deemed unnecessary (borderline skin test sensitivity and/or no life-threatening SR), and were resting in the field, and (2) if a subject experienced only LR's after previous stings, were either VST positive or negative, were not receiving venom therapy, and were later stung in the field.

This first study presented demographics and history-sting data for the 3236 HVS subjects. Local reactions, skin test results, and adverse reactions to skin testing and to venom immunotherapy will be analyzed in future articles.

MATERIAL AND METHODS

Participation of physicians in the HVS was solicited at the 1979 AAAI meeting and by letter from the Insect Sting Committee of the Academy requesting participation from directors of training programs in allergy and immunology. Letters to participating physicians made the following specific requests: (1) submit data on all subjects initially evaluated or who had received WBE and had been reevaluated for Hymenoptera insect allergy, (2) delegate one individual to complete the questionnaires of the protocols, (3) perform skin testing according to enclosed commercial standard instructions with 0.05 ml of extract for each intradermal test dose, (4) follow the treatment schedule provided in the

TABLE I. SRI*

Severe	
Unconsciousness	0.376
Shock	0.376
Drop in blood pressure	0.126
Moderate	
Lower airway obstruction	0.050
Upper airway obstruction	0.050
Gastrointestinal symptoms	0.013
Mild	
Angioedema/urticaria	0.003
Pruritus	0.003
Other	0.003
Possible total	1.000

*See text for explanation.

commercial venom-extract package insert, (5) include in the study subjects who had been receiving WBE but exclude those continuing therapy with WBE, and (6) promptly complete and return follow-up forms that would be initially scheduled at 6 months, then 1 year, and yearly thereafter.

A five-page questionnaire (entry forms 1 through 5) and instructions were sent to participating physicians for each subject. The questionnaires were supplied in duplicate on two-part National Cash Register (Dayton, Ohio) carbonless paper. The responder was to supply appropriate information for each question, respond "unknown" or leave the response area blank; blank spaces were entered into the data base as "unknown" or "missing."

Entry forms 1 and 2 consisted of two parts:

Part I, Subject Identification. Demographic and relevant historical data requested whether the subject was currently a beekeeper, whether there was an atopic history (hay fever, atopic eczema, and/or asthma), and information about WBE treatment in the past.

Part II, Insect-sting History. The time and characteristics of the subject's MRSPEs was requested and whether this sting had caused an LR and/or an SR. The time from sting to maximum LR and size of any LR was requested. LR's were defined as visible reactions at the site of the historical sting. LLR's were defined as any visible LR ≥ 2 inches in diameter. Also requested were whether any of the following systemic symptoms and signs occurred; generalized pruritus, cutaneous angioedema and/or urticaria, upper airway obstruction (primarily as laryngeal edema), lower airway obstruction, drop in blood pressure, gastrointestinal symptoms (vomiting, diarrhea, and/or abdominal colic), unconsciousness, shock, or "other." When "other" was affirmed, the responder was asked to write in a description of symptom(s). The judgment of the attending physician was relied on for determining whether such symptoms as a drop in blood pressure, unconsciousness, or shock warranted a positive report. No detailed explanations of terms was provided in the questionnaires. Details of any occurrence of reactions to the imported fire ant and/or other ant stings, if they were available, were also requested.

TABLE II. Characteristics of HVS subjects

	N	Age (yr)				Age not reported (%)	Sex		Race		
		Mean age	<17 (%)	17-39 (%)	>39 (%)		M (%)	F (%)	White (%)	Black (%)	Other (%)
Total subjects	3236	30.5	31.8	33.9	30.4	3.9	61.5	38.5	95.4	2.0	2.6
SR in Hx*	2866	30.6	31.9	33.2	30.8	4.1	62.4	37.6	95.4	2.0	2.6
SR in Hx and positive skin test†	2181	30.1	32.0	34.2	29.7	4.1	64.7	35.3	96.0	1.5	2.5
SR in Hx and negative skin tests	685	31.9	31.4	29.9	34.5	4.2	54.7	45.3	93.7	3.6	2.7

Boxed figures are referenced in text; Hx = history.

*Three hundred seventy subjects had a local reaction or large local reaction in their history and no reported systemic reaction.

†Venom skin test data will be reported in a future article.

TABLE III. Total subjects (3236) and participating physicians (84) by region* (percent)

	Northeast (%)	Northcentral (%)	Southeast (%)	Northwest (%)	Southcentral (%)	Southwest (%)	Canada (%)	Other (%)
Subjects	28.3	13.5	21.1	8.8	6.1	12.3	9.8	0.1
Physicians	32.9	18.8	23.6	3.5	5.9	10.6	4.7	

Boxed figures are referenced in text.

*Northeast: New Jersey, New Hampshire, Connecticut, Pennsylvania, New York, and Massachusetts.

Northcentral: Indiana, Minnesota, Michigan, Illinois, Iowa, Ohio, and Kansas.

Southeast: Florida, Maryland, Tennessee, Washington, D.C., Georgia, Louisiana, Kentucky, West Virginia, and Virginia.

Northwest: Oregon and Washington.

Southcentral: Texas and Oklahoma.

Southwest: Arizona and California.

Canada: Toronto, Ontario area.

Entry form 2 of the subject questionnaire requested the same information as the Insect-sting History, summarized in reverse chronologic order, for all known stings on record or reported by subjects from memory. In some cases, it was not possible to obtain accurate data for all historical stings.

Entry forms 3 and 4 outlined the methods of prick skin testing with venoms, with histamine as a control, and when to do intradermal skin tests and scoring and recording of these tests. Physicians were requested to follow instructions for skin testing in the package insert accompanying venoms. Skin test reactions were measured in 15 minutes, and the sums of the longest diameter and midpoint perpendicular diameter for both erythemas and wheals produced by each type of venom were recorded. Data on late-phase reactions were not requested.

Entry form 5 recorded the presence or absence of an SR during VST. If an SR occurred, symptoms and signs were recorded as on forms 1 and 2, part II (Insect-sting History). If the attending physician intended to treat a subject with venom immunotherapy, that subject was entered into the

Therapeutic Safety and Efficacy Protocol. Otherwise, the subject entered the Diagnostic Efficacy Protocol.

Appropriate follow-up forms were initially mailed to physicians at 6 and 12 months after a subject had entered the study and every 12 months thereafter. The follow-up data for treatments and reactions occurring through December 1982 were entered into the data base providing a 3-year study period. Any submitted data that pertained to treatment or stings that occurred after the study period were filed but not considered part of the HVS data base. If the subject was to be treated with venom therapy, scheduled Therapeutic Safety and Efficacy Protocol follow-up forms were provided to physicians; if they were not, Diagnostic Efficacy Protocol follow-up forms were provided according to schedule.

Therapeutic Safety and Efficacy Protocol follow-up forms consisted of three sections: form A, Venom Therapy; form B, Treatment Reaction report; and form C, Insect-sting follow-up.

The Venom Therapy section, form A, requested the sub-

Personal Hx of atopy (%)	Before treatment with WBE (%)	Hx as beekeeper (%)
32.3	42.0	3.1
31.2	43.1	3.0
29.5	43.4	3.3
36.8	42.2	1.8

ject's name, physician's name, and date of entry into the study. Physicians added the date of report, the dates of both the first and most recent venom dose, the date when immunotherapy reached maintenance (at least 100 µg for a specific venom), and the treatment date indicated on the most recently submitted previous report. Details of the current dose included the venom(s) injected, volume(s), manufacturer(s), concentration(s) in micrograms per milliliter, whether the subject was continuing venom therapy, and, if treatment was to be stopped, the reason and date when treatment was stopped. Form A also requested whether the subject had experienced an SR or any serious reaction during immunotherapy since the original or latest previous report.

If a reaction attributable to immunotherapy had occurred, completion of a Treatment Reaction report (form B) was requested. Form B recorded the date of the most recent reaction associated with venom immunotherapy and whether this was an anaphylactic reaction (SR) or a nonanaphylactic reaction, such as serum sickness or vasculitis. The same SR symptoms requested in part II (Insect-sting History) of the HVS entry forms were to be reported, if they were present. The identities of the venom(s), volume(s), concentration(s), manufacturer(s), and lot number(s) were also reported.

Form C, the Insect-sting History follow-up, was to be completed for any Therapeutic Safety and Efficacy Protocol follow-up subject who had been stung since the date of the last previous report. Questions on this form concerned the date of the last insect-sting reaction, stinging insect, number of stings, peak size of any LR, time to peak LR, and size of this LR compared to any immediately prior LR. Also requested was whether an SR followed the sting (with or without LR), time (minutes) from sting to first systemic symptom, whether epinephrine had been administered, comparison of the severity of this SR to prior SR(s), and information on the presence or absence of the same signs and symptoms as reported on other report forms.

Form X, the Diagnostic Efficacy Protocol follow-up form, was also mailed to participating physicians for those HVS subjects being followed but not receiving immunotherapy. This form requested the same information as form C (Insect-sting History follow-up).

Forms D and E were provided to physicians in quantity to report occurrences of reactions to immunotherapy or in-

field stings occurring between scheduled follow-up reports. Form D was used to report adverse reactions to immunotherapy with format identical to form B. Form E was for reporting reactions to insect stings in a format identical to form C and was used for both HVS protocols.

Each participating physician received a supply of postcards that were to be sent to those of his subjects who had been entered into the study but were not observed regularly. These postcards asked whether the subject had been stung since the last request for data and if there had been any LR or SR. Subjects who had been stung were requested to contact their physician's office to provide details of the sting for inclusion in the study-data files.

The Therapeutic Safety and Efficacy Protocol includes all subjects who were treated with immunotherapy at any time during the study. Most of the treated subjects were skin test positive for at least one test venom. The criteria for a positive response, with or without an SR, is the sum of wheal cross diameters of at least 10 mm and the sum of erythema cross diameters of at least 22 mm (both conditions must be present). A few subjects, not meeting the above skin test criteria and/or not having previously experienced an SSR, were included in the HVS by their physician and treated with venom immunotherapy. These subjects, in future studies, will be considered separately from those who fulfill the skin test positive criteria.

An explanation of every subject lost from the study had not been requested originally but was requested later in the study. A letter was sent to all physicians who had subjects with incomplete files requesting follow-up data and an explanation concerning any subject who had been lost to follow-up.

The computing facilities of the University of South Florida were used for data storage and subsequent analysis. This system is an IBM (International Business Machines Corp., Armonk, N.Y.) 3081 mainframe computer with extensive capabilities and many available languages and systems. The Statistical Analysis System (registered trademark of the SAS Institute, Inc., Cary, N.C.) was used for most data analysis. An information management system has been designed to store and facilitate analysis of the approximately 42,000 pages of data representing approximately 5.5 million pieces of information in the HVS.

The SRI is a numerical scale devised for the ranking of the severity of SRs (Table I). Unconsciousness, shock, and a drop in blood pressure are considered to be the most severe reactions. A nonshocking drop in blood pressure is not considered as severe as the other two. Moderately ranked signs or symptoms are lower or upper airway obstruction and/or gastrointestinal symptoms, the latter not considered as severe as the other two. Angioedema and/or urticaria, pruritus, and/or "other" symptoms are considered to be mild. These differences are reflected in the values assigned to each. The SRI was designed so that the sums of values for a mild reaction would not equal the lowest value of a moderate reaction, and the sum of values of a moderate reaction, either alone or in conjunction with a mild reaction, would not equal the value of the least severe reaction (drop in blood pressure).

TABLE IV. Number of subjects and type of reaction to most recent sting before entry into study (MRSPES)

Stinging insect	Absence of SR to MRSPES	SR				Moderate/severe subtotal	Total
		Mild	Moderate	Severe			
Honeybee	242	141	193	+	91	= 284	425
Wasp	156	91	128	+	82	= 210	301
Yellow jacket	206	214	218	+	160	= 431	592
White-faced hornet	10	12	19	+	13		44
Yellow hornet	16	9	11	+	10		30
Imported fire ant	14	3	5		10		18
Other ant	8	1	1		2		4
Unknown un-reported	365	307	296		202		805
Total	1017 (31%) †		65%				2219

Boxed figures referenced in text.

*Less than 1%.

†647 (64%) of these subjects experienced at least one systemic reaction to a prior sting.

‡731 of these subjects experienced at least one systemic reaction to a prior sting (23% of total subjects or 33% of subjects with a systemic reaction from most recent sting before entry into the study).

§Three hundred seventy subjects had never experienced a systemic reaction; 2866 (89%) of all Hymenoptera venom study subjects had a systemic reaction in history.

TABLE V. Number of subjects and type of reaction to most recent sting before entry into study

Reported No. of stings incurred per sting episode	Non-SR	SR				Moderate/severe as % of total	Total
		Mild	Moderate	Severe	Total		
1	832	591	690	415	1696	65	2528
2	49	59	65	48	172	66	221
3	21	23	26	22	71	68	92
4-10	40	55	46	39	140	61	180
>10	8	13	13	17	43	70	51
Unknown/unreported	67	37	31	29	97	62	164
Total	1017				2219		3236*

Boxed figures are referenced in text.

*Three hundred seventy subjects had never experienced a systemic reaction.

RESULTS

The age distribution, sex, race, history of atopy, prior history of WBE treatment, and beekeeper status are presented in Table II. The mean age (years) was 30½ with a range of 1 to 83 years. Male subjects accounted for 61.5% and female subjects, 38.5%.

Ninety-five percent were white, 32% were atopic, and 42% had prior WBE treatment. Beekeepers accounted for 3% of the sample. Demographic data for the 2866 subjects with a historical SR, the 2181 subjects with both a historical SR and a positive skin test, and the 685 subjects with a historical SR and negative skin

Moderate/severe as % total	Total as % N (N = 2219)	Total by insect
$\frac{284}{425}$ 67%	19	667
$\frac{210}{301}$ 70%	14	457
Total		798
= $\frac{431}{666}$ 65%	30	54
83%	1	46
75%	*	12
62%	36	1170
(69%) ‡		3236 §

tests were similar and also are presented in Table II. There was an average of 2.7 history sting episodes per subject (not in Table II).

The regional distribution of subjects and physicians contributing data is presented in Table III. Most subjects (63%) and reporting physicians (75%) came from the northeast, northcentral, and southeast sections of the United States.

The number of subjects, the severity of the SR after the MRSPES, and the stinging insect implicated in the reaction are presented in Table IV. Of the 3236 subjects surveyed, 2219 (69%) experienced an SR after the MRSPES. Seven hundred thirty-one of these subjects (23% of the total subjects or 33% of those with an SR from the MRSPES) had experienced at least one SR to a prior sting. In contrast, 1017 (31%) of the stung subjects had not experienced an SR from the MRSPES. Of these 1017 subjects, 647 (64%) had experienced an SR to a prior sting. Moderate to severe SRs were equally likely after stings of the yellow jacket, white-faced hornet, yellow hornet (431/666 or 65%), honeybee (284/425 or 67%), or wasp (210/301 or 70%). SRs, regardless of severity, were noted more often after stings of the yellow jacket, white-faced hornet, or yellow hornet (30%) than after honeybee (19%) or wasp stings (14%).

The relationship between the number of stings and the reaction severity to MRSPES is presented in Table V. Moderate to severe SRs were no more likely if the subject was stung once (65%) or four to 10 times (61%) during the same episode.

Of the 2219 subjects who reported an SR from the MRSPES, 2126 provided sufficient information to determine their age at *time of study entry*, although specific age at the time of MRSPES was not requested (Table VI). Of those subjects in the group younger than 17 years of age, 44% had mild; 44%, moderate; and 12%, severe SRs. Of the 17- to 39-year-old age group, 33% had mild; 41%, moderate; and 26%, severe SRs. Of the group older than 39 years of age, 29% had mild; 33%, moderate; and 38%, severe SRs. The percentages of the sample in the three age groups were similar: younger than 17 years, 33%; 17 to 39 years, 36%; and older than 39 years, 31% (Table VI). The incidence of SR from MRSPES for all age groups were mild, 35%; moderate, 39%; and severe, 25%. Fifty-six percent of subjects aged 17 years or younger with an SR from the MRSPES had an SR in the moderate/severe ranges, whereas 67% of the 17- to 39-year-old age group and 71% of the group older than 39 years also experienced a moderate/severe SR.

The total number of history SSRs experienced by each subject is presented in Table VII. Of the 3236 subjects surveyed, 2866 (89%) reported at least one historical SR. Most subjects reported experiencing only a single SR (70%); however, approximately 9% of the population reported experiencing three or more of these reactions. This latter figure could be subject to error from insufficient data, since some physicians did not list all historical SRs or did not list more than a certain number. Data on historical SRs, other than those associated with the MRSPES, were not analyzed in detail because it was not possible to obtain accurate information for all historical stings.

The time to onset of the SRs is presented in Table VIII. Fifty-one percent of the SRs after the MRSPES occurred in 10 minutes or less. Eighty-six percent of the SRs from the MRSPES began within 1 hour. (Nine percent were unknown or unreported.) A large number of SRs occurring in 10 minutes or less were moderate to severe (72%) in comparison to mild reactions (28%) occurring during this same time period. There was a gradual decrease in the frequency of moderate to severe reactions when the time of onset exceeded 10 minutes, for example, 63% at 11 to 20 minutes onset that declined to 42% at 301 to 2880 minutes onset. Four severe reactions began at 301 or more minutes.

The number of subjects who received epinephrine after the MRSPES that yielded an SR and the severity of the SRs are presented in Table IX. Subjects reporting moderate to severe SRs were somewhat more likely to have received epinephrine (80%) than subjects reporting mild SRs (64%). Of 2219 experiencing SRs on the MRSPES, 68% had received epinephrine.

The relation between the severity of the most recent

TABLE VI. Number of subjects with MRSPES yielding an SR

	SR			Row total	% Moderate/severe	% Total (N = 2126)	% Total (N = 2219)
	Mild	Moderate	Severe				
Age at study entry (yr)							
<17	309 (44%)	305 (44%)	86 (12%)	700	56	33	32
17-39	251 (33%)	312 (41%)	197 (26%)	760	67	36	34
>39	191 (29%)	222 (33%)	253 (38%)	666	71	31	30
Subtotal	751 (35%)	839 (39%)	536 (25%)	2126			
Unknown/unreported age at study entry	27	32	34	93	71		4
Total	778 (35%)	871 (39%)	570 (26%)	2219			

Boxed figures are referenced in text.

TABLE VII. Total number of SRs reported per subject by subjects having a history of sting(s) with SRs

No. of SRs*	No. of subjects	% (N = 2866)
1	2015	70.30
2	581	20.27
3	179	6.25
4	45	1.57
5	28	0.97
6	10	0.35
7	3	0.11
8	1	0.04
9	2	0.07
10	2	0.07
Total	2866 (89%)	100.00

Boxed figures referenced in text.

*Some physicians indicated they ceased to collect history-sting data after four or five reports of history stings.

SR and an immediately prior SR is presented in Table X. Subjects with moderate to severe SRs from the MRSPES and a history of prior SR(s) were more likely to report the current reaction as equal or more severe than the prior reaction (76%), compared to subjects with mild reactions (55%). In 66% of SRs after the MRSPES, there had been no prior SR.

DISCUSSION

This study of the experience with venom-sensitive subjects by the membership of the AAAI that followed the licensure of standardized venoms of Hymenoptera (bee, yellow jacket, white-faced hornet, yellow hor-

net, and wasp) in 1979 represents the largest sample of sting-allergic subjects ever evaluated.

The demographic characteristics of this sample (Table II) are similar to samples of sting-allergic subjects previously surveyed (Table XI). Note that the mean age (30.5 years for all HVS subjects and 30.6 years for those with a history of an SR), male subject percentage (62%), and percent who are atopic (32% and 31%, respectively, for all HVS subjects and those with a historical SSR) are similar to the tabulated mean age (28.6 years), male subject percentage (64.2%), and percent atopic (29.3%) in the cited studies.¹⁻⁶ This indicates that the HVS sample is typical of sting-allergic subjects previously studied. The male subject predominance has also been observed in prior studies of pediatric,^{6,7} and young adult samples.¹⁴ This male subject predominance is much greater than that observed for hypersensitivity to several common aeroallergens,⁸ suggesting that the immune response to venom allergens is particularly intense in male subjects or that the degree of exposure and/or reported stings from Hymenoptera is significantly greater for male subjects compared to female subjects.

There were no reported fatalities among HVS subjects attributable to insect stings, skin testing, and treatment during the course of the HVS. When the HVS subject characteristics are compared to subject characteristics in other studies where subjects experienced fatal reactions to Hymenoptera stings (Table XII), the mean age (47 years) and male subject predominance (78%) of the deceased subjects in the cited references are higher than for the average age (30.5 years for all subjects and 30.6 years for subjects with an historical SR) and percent of male subjects (61.5%) in the HVS.⁹⁻¹² The reason for this is unclear.

TABLE VIII. Time to SR

Time (min) to SR	Frequencies of SRs reported before MRSPES	No. of subjects with MRSPES yielding an SR						% Total (N = 2219)	Total SR Hx
		Mild	Moderate	Severe	Total	Moderate/ severe as % of total			
0-10	850	317 (28%)	435	377	1129	72	51	86%	1979
11-20	413	165	187	88	440	63	20		853
21-40	162	84	94	46	224	63	10		386
41-60	100	48	44	16	108	56	5		208
61-120	33	22	20	6	48	54	2		81
121-300	22	13	11	2	26	50	1	48	
301-2880*	39	18	10	3	31 (4)	42	1	70	
> 2880	5	6	0	1		7	14	†	12
Unknown/unreported	318	105	70	31	206	49	9	524	
Total	1942‡				2219			4161	

Boxed figures are referenced in text; Hx = history.

*Four of the severe reactions began at 301 or more minutes.

†Less than 1%.

‡This data not analyzed in detail because of questionable historical accuracy.

TABLE IX. Epinephrine use and SR severity

Epinephrine administered	No. of subjects with MRSPES yielding an SR									
	Mild		Moderate		Severe		Combined moderate/ severe		Total	
	N	%	N	%	N	%	N	%	N	%
Yes (before/during the SR)	454	64	596	74	457	88	1053	80	1507	68
No	251	36	208	26	63	12	271	20	522	24
Total	705		804		520		1324			
Unknown/unreported	73		67		50				190	8
Total									2219	

Boxed figures are referenced in text.

The high percentage of subjects previously treated with WBE (42%) is consistent with prior studies,^{4, 13} reflecting the widespread use of WBE for therapy before the availability of venoms.

Blacks, in this survey, accounted for 2% of the sample, the same percentage of blacks reported in a previous review.¹⁴ This low percentage contrasts with the higher prevalence of immediate hypersensitivity to common aeroallergens of blacks compared to whites in the U.S. population.⁸ One possible explanation is that the physicians from whose practices the

data on sting-allergic subjects were submitted did not have access to the black sting-allergic population. It is also possible that the black population is either not exposed as often to Hymenoptera stings or does not develop hypersensitivity to venom proteins as readily as do whites. This observation merits further study.

The percentage of sting-allergic subjects in the HVS who are also atopic (Table XI) is in agreement with the tabulated data reported in some other studies, although atopy is not uniformly defined among studies. The higher incidence of atopy in the HVS than in the

TABLE X. Most recent sting with SR compared to immediate prior sting with SR

This SR compared to immediate prior SR*	No. of subjects with MRSPEs yielding an SR					% Total (N = 437)	Total	% Total (N = 2219)
	Mild	% Total (N = 168)	Moderate	Severe	Combined moderate/severe			
Less severe	76	45	81	22	103	24	179	8
Same	54	55	65	44	109	76	163	7
More severe	38		120	105	225		263	12
Subtotal	168		266	171	437		605	
No prior SR	557		550	366			1473	66
Unknown/unreported	53		55	33			141	6
Total	778		871	570	437		2219	

Boxed figures are referenced in text.

*In comparing a systemic reaction to the immediate prior systemic reaction, it is important to note that the "no prior systemic reaction" option would be marked by the respondent when a particular reaction is the first one experienced. Also, an individual may have previously experienced several systemic reactions in the past.

TABLE XI. Age, sex, and personal history of atopy of sting-allergic subjects studied in prior decade

Reference	No. of subjects	Prior reported sting Hx	Mean age	Age (yr) range	Sex (%)		Hx of atopy (%)
					M	F	
Present study	3236	Any local or SR	30.5	1-83	62	38	32*
Present study	2866	SR	30.6	1-83	62	38	31*
1978 ¹	119	SR	27	2-73	65	35	25†
1983 ²	458	SR	NA	NA	NA	NA	14‡
1983 ³	67	SR	34	NA	59	41	28
1982 ⁴	21	5 LLRs, 16 SRs	28	7-58	52	48	NA
1978 ⁵	59	SR	39	15-63	68	32	NA
1985 ⁶	98	SR	15	2-52	77	23	50§
Tabulated averages			28.6		64.2	35.8	29.3

Boxed figures referred to in text; Hx = history; NA = not available.

*Asthma, allergic rhinitis, and atopic eczema.

†Asthma and rhinitis.

‡Not defined.

§Positive prick skin test to nonvenom allergens.

||Hay fever, asthma, and "other specific incidence of atopy."

general population is most likely due to subject selection and might be expected, since all the reporting physicians were allergists/immunologists and subjects were selected from their patients. Other studies have demonstrated that the prevalence of atopy among nonsting-allergic subjects is not appreciably different from the prevalence of atopy among sting-allergic subjects.¹⁻³

The proportion of subjects entered from various regions of the United States, especially the eastern United States (63% from the northeast, northcentral,

and southeast combined), either reflects the large proportion of physicians submitting data (75% from these areas, Table III) or indicates a real regional difference in the prevalence of sting allergy. A high percentage of fatalities caused by insect stings has been previously reported from the eastern United States.¹⁵

An SR after the MRSPEs was experienced by 2219 (69%) of the 3236 subjects of the HVS, and 65% of these reactions were moderate to severe (Table IV). Eighty-nine percent (Table VII) of the HVS subjects reported a previous SSR, 63% (not presented in Table

TABLE XII. Hymenoptera sting fatalities*

Reference	No of fatalities	Mean age (yr)	Range (yr)	Sex (%)	
				M	F
1984 ⁹	25	34	<5 to >50	80	20
1983 ¹⁰	26	53	0.5 to 84	73	27
1962 ¹¹	28	47	1 to 84	NA	NA
1963 ¹¹	25	50	25 to 85	NA	NA
1984 ¹²	48	50	<1 to 84	81	19
Tabulated averages	30.4		46.5	78	22

Boxed figures referred to in text; NA = not available.

*Bee, vespid, and wasp.

VII) of which were of moderate or severe degree. Similar results were encountered in an AAAI survey of 2606 subjects.¹⁶ Eighty-seven percent of that sample had experienced a prior SR (not necessarily after their most recent sting), and 68% of these SRs were classified of moderate or severe intensity. This prevalence of moderate/severe SSRs (excluding cutaneous reactions only) observed in both studies differs from one study of children (younger than 16 years of age) that reported 68% of subjects with SSRs had only mild (cutaneous) reactions.⁷

The earlier survey by the AAAI reported that the most frequently implicated insect was yellow jacket, followed by honeybee and wasp.¹⁶ The findings of the HVS were similar (Table IV). The frequency of the incriminated insect, however, depends on the regional prevalence of these insects and/or on correct identification by the stung subject.³ There was no correlation between the reported severity of the SSR and the number of stings, suggesting that cumulative effects of venom are not apparent when 10 or fewer stings are received and that the allergic response is just as likely to be maximal after a single sting versus up to 10 stings at the same time (Table V).

This study indicates that the younger population, younger than 17 years, reported fewer severe SSRs (12%) associated with the MRSPES than either subjects 17 to 39 years of age (26%) or the older population, older than 39 years (38%) (Table VI). This suggests that the older population (1) may be more sensitive than the younger population, (2) cannot as readily withstand the cardiovascular and/or pulmonary complications of anaphylaxis, or (3) are more refractory to emergency treatment measures. Fifty-six percent of the group younger than 17 years had moderate or severe reactions as compared with 71% of the group older than 39 years. Therefore, 44% of the group younger than 17 years had mild reactions, which

is considerably lower than the 68% prevalence of mild systemic reactions for patients with a mean age of 9.3 years reported by Schubert et al.⁷

Seventy percent of the HVS subjects reported experiencing only one SSR (Table VII). Most SRs after the MRSPES (51%) occurred within 10 minutes of the sting, as well as a high percentage (72%) of the moderate to severe SRs during this same time period (Table VIII). Subjects who experience symptoms immediately after a sting must be administered emergency care as soon as possible. It is also important to note that moderate to severe reactions may occur hours after a sting; four moderate or severe reactions among HVS subjects began 301 or more minutes after sting(s).

The intensity of some SSRs may have been modified by the prompt and frequent use of epinephrine (Table IX). Eighty-eight percent of subjects reporting a severe SR associated with the MRSPES received epinephrine. The frequency of use of epinephrine in this study is higher than that observed in the prior AAAI survey in which <38% of the sting-allergic subjects who were restung received epinephrine.¹⁶ This suggests more effective physician and subject education regarding the emergency use of epinephrine. These figures are still lower than what they should be and indicate that the favorable increase in the use of epinephrine that has been accomplished by education since 1965 needs amplification.

Most subjects (66%) with moderate to severe SRs to the MRSPES had no history of a prior SSR, a percentage that is almost identical to the 65% reported in the previous AAAI survey.¹⁶ Subjects with a previous history of SSRs of moderate to severe intensity were in the majority (76%) and were more likely to classify the severity of their most recent reactions as equal to, or more intense than, their previous SSRs (Table X). Whether these reactions were more severe

or perceived to be so due to their recency cannot be determined from this survey. The data suggest that a second SSR will be of the same intensity or worse in most cases.

Future analyses of the HVS will address other questions, such as subjects' skin sensitivity and adverse reactions after skin testing and venom immunotherapy.

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