

Nonfatal results in third-degree anaphylaxis from Hymenoptera stings

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Clinical data obtained from 100 cases of severe anaphylactic reactions to one or more Hymenoptera stings are presented. Comparisons are shown with 50 fatal cases resulting from one or more Hymenoptera stings who were autopsied. Ancillary data from the 2 groups covering types and numbers of insects involved, ages of the patients, sites of stings, speed of onset of reaction, and other features showed no striking differences. In the recovered cases, 97 per cent developed systemic symptoms within an hour after the sting and 3 per cent after the first hour. Speed of onset of reaction is mostly unknown for the fatal group, but 62 per cent of them died within the first hour after the sting, leaving 38 per cent who died more than one hour after the sting. Eighty-seven per cent of the recovered cases received treatment within an hour from the time of stings. In the fatal cases, inadequate or no treatment was the rule. Epinephrine was given to 67 per cent of the recovered patients, and data regarding all drugs used are tabulated. The most frequent types of systemic reactions in the nonfatal group were general urticaria (74 per cent), syncope (65 per cent), and respiratory tract obstruction (38 per cent). Conclusions: Treatment at the earliest moment after systemic symptoms appear is needed; epinephrine has been uniformly successful in the large number receiving it in this series; the need for insect-sensitive persons to be trained to give epinephrine and other medications in an emergency is evident.

In 1967, the Subcommittee on Insect Deaths from Hymenoptera stings of the American Academy of Allergy reported autopsy findings on 50 such fatal reactions.¹ This report is a study of 100 nonfatal cases of potentially life-threatening or third-degree reactions from Hymenoptera stings selected from 140 patients submitted by 22 members of our study group. Comparisons are made between the fatal and nonfatal series to find explanations for the difference in outcome.

CLINICAL DATA

The types of the reactions in both series were mainly similar. In this series these included massive tissue edema (74 per cent), syncope (65 per cent), respiratory tract obstruction (38 per cent), and vascular collapse (19 per cent)

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(Table I). Symptoms suggestive of delayed reactions from hemorrhage in various tissues, severe pulmonary congestion, and nerve tissue destruction, as found in fatal cases,²⁻¹⁰ were not encountered in this nonfatal series.

The phrase "third-degree anaphylaxis" is used to indicate the most severe reaction from one or more Hymenoptera stings which was compatible with life. Data which follow strongly suggest that early appropriate treatment prevented a number of these nonfatal cases from progressing to a fatal termination. The first- and second-degree systemic reactions were slight to moderate complaints of urticaria and angioedema, tingling, weakness, sweating, blurred vision, nausea, palpitation, apprehension, throat irritation, tightness in chest, and wheeze. Studies of these case histories and personal experiences with similar patients indicate the third-degree reaction could be life-threatening. The fatal cases might well be classified as fourth-degree reactions. Table II shows additional symptoms and signs observed in the 100 nonfatal cases.

Clinical data, such as ages of patients, site of stings, and types and numbers of insects, were carefully compared in the fatal and nonfatal groups. They are omitted because they show no outstanding differences between the two groups.

Table I. *Degrees of systemic reactions to Hymenoptera stings*

Reactions	Degree		
	1st	2nd	3rd
Urticaria and angioedema	Slight, generalized	Moderate	100 Recovered cases; 74% severe-massive
Syncope	Slight warning signs*	Moderate warning signs*	65% varying periods of coma (minutes to over 1 hour)
Respiratory obstruction	Slight warning signs†	Moderate warning signs†	38% severe
Vascular collapse	Slight warning signs*	Moderate warning signs*	19% severe

*Tingling, weakness, sweating, blurred vision, nausea, apprehension, palpitation.

†Palpitation, apprehension, throat irritation, tightness in chest, wheeze, dyspnea.

Table II. *Clinical histories in nonfatal Hymenoptera stings*

Important symptoms after sting	%	Other symptoms or signs after sting	%
Giant urticaria with pruritus and flushing	74	GI symptoms including nausea and vomiting	16
Syncope	65	Vertigo	12
Wheeze, dyspnea, and choking	38	Fall in blood pressure	11
Presyncope*	26	No pulse	6
		No blood pressure	2

*Weakness, sweating, pallor, tingling, apprehension, blurred vision.

Table III shows an important difference between the two series in that over 97 per cent of the recovered cases had the onset of the reaction in the first hour and the remaining 2.6 per cent developed symptoms within 6 hours after the sting. In comparison, only 62 per cent of the fatal cases developed symptoms within 60 minutes of the sting or stings. Twenty-four per cent of the fatal-case reactions began between one and 24 hours after stings. Most importantly, we find 14 per cent of the fatal cases started systemic reactions after 24 hours.

Table IV shows another striking difference between the two groups in that 87 per cent of recovered cases received some form of medication, mostly anti-allergic, within the first hour after being stung. In comparison, only 6 per cent of the 50 fatalities received treatment in the same period. In 2 of these 3 cases, treatment appeared inadequate. In 9 (18 per cent) additional fatal cases, death was possibly due to delay in starting treatment. Of the 8 recovered patients who received no treatment, 7 were in coma from 3 minutes to one hour. This indicates that patients with severe anaphylactic reactions can survive without treatment, but there is no way of choosing which patients can live through such a test. Several untreated patients have died during a long wait for an ambulance.

Table V shows the medications most frequently used in the 100 recovered cases, i.e., epinephrine, antihistamines, steroids, and oxygen. Aqueous epinephrine has been the emergency measure employed most often. The table also shows various medications less frequently used. An important finding relating to the treatment of patients with these nonfatal reactions was that there was no apparent need for further treatment once the reaction had been brought under control. This differs from some of the fatal reactions where there was a delayed onset of symptoms in 38 per cent of the cases, varying from one to over 24 hours.

Table VI shows that 36 per cent of the recovered cases had a positive personal history of allergy other than from insect stings, and 33 per cent had previously experienced reactions from Hymenoptera stings. In the fatal-case series, information about patient allergy was known in only 12 cases. It was noteworthy that in 30 cases there was a negative personal and family allergic history, including no previous reaction to stings, indicating that these are not dependable criteria for anticipating reactions. These patients had third-degree reactions to a single sting between 20 minutes and one hour in all but one case.

There was a variable severity of response to stings in 6 of the cases who had a previous positive personal insect-sting history in this recovery group of 100 cases. These persons previously had third-degree reactions and then only mild local or systemic symptoms prior to the present, severe one. For example, one patient had a similar severe, then a milder reaction, before his present one when he was in coma for one hour from 20 yellow jacket stings before epinephrine was given with prompt recovery.

DISCUSSION AND CONCLUSIONS

Third-degree reactions from Hymenoptera stings, including severe angioedema, syncope, respiratory tract obstruction, and vascular collapse, are life-

Table III. *Comparison of clinical data in nonfatal and fatal Hymenoptera stings*

Cases	Time of onset of reaction after sting				
	Minutes		Hours		
	0-30	30-60	1-6	6-24	24+
100 Recovered	96%	1.4%	2.6%	—	—
50 Fatal	38%	24 %	22 %	2%	14%

Table IV. *Time from sting to beginning of treatment*

Cases	0-10 min.	10-30 min.	30-60 min.	Over 60 min.	No treatment	No information
100 Recovered	15%	22%	50%	4%	8%	1%
50 Fatal	0%	0%	6%	18%	66%	10%

Table V. *Medications used in nonfatal Hymenoptera stings*

Frequently used	Infrequently used	Others
Aqueous epinephrine injections, 67 %	Infusions, 5 %	Calcium, morphine,
Antihistamines (injection or oral), 21 %	Isoproterenol, 4 %	demerol, aramine,
Steroids, 14 %	Aminophylline, 2 %	others listed as
Oxygen, 10 %	Ephedrine and deriv.	"pills and injections"
	2 %	

In 8 cases no treatment was given.

Table VI. *Comparison of allergic histories in recovered and fatal reactions to Hymenoptera stings*

Cases	History				
	Positive past personal		Positive family	None	Unknown
	Insect sting	Other allergies*			
100 Recovered	33	36	11	30	3
50 Fatal	6	3	Unknown	3	38

*Number of cases: hay fever, 14; urticaria, 9; perennial rhinitis, 9; food, 2; asthma, 1; tetanus antitoxin, 1.

threatening. Similar symptoms occurred in 50 patients prior to their death. Important differences were found between the two groups: in the recovered series over 97 per cent of the reactions occurred within an hour after the sting, and all developed trouble within 6 hours from the stings; 87 per cent of the recovered series received medication, mostly antiallergic, within the first hour.

In the fatal series, 62 per cent of the reactions started within the first hour and only 6 per cent received treatment prior to death. Reactions in 24 per cent began between one and 24 hours and in 14 per cent after 24 hours. The fatal reaction in those patients whose symptoms began after 24 hours was believed due to delay in start of treatment, inadequate therapy, or no treatment. Serious

delayed reactions to stings were discussed by the author in 1966.¹⁰ The possibility that delayed hypersensitivity may have been involved in the delayed fatal cases was considered. This possibility is supported by delayed skin test reactions in some instances. However, the postmortem findings in 12 of 19 patients with delayed deaths showed respiratory tract pathology; these patients could have fallen into the respiratory obstruction category of the recovery series. Another 4 of these 19 showed extensive vascular damage, and the remaining showed severe nervous system damage with death after prolonged therapy. Hemorrhagic and vascular lesions also suggest Arthus-type hypersensitivity, a possibility which has received scant attention.

The choice of medication was epinephrine in 67 per cent of the cases. Early treatment is needed. Further therapy was rarely required after the initial reaction had been controlled. The need for insect-sensitive persons to have available and to be trained in giving epinephrine, antihistamines, and steroids is self evident.

The following physicians contributed data to this study: Drs. Ian Ajac, James Barnard, Roman Bladdek, Halla Brown, Alan Cazort, Francis Chafee, Sheldon Cohen, William Cohen, Monroe Coleman, Herbert Dieckman, Richard Farr, Eloise Kailin, Macy Levine, Kenneth Mathews, Harry Mueller, Charles Reed, Jourdan Roane, John Stevens, Joel Teigland, John Toogood, Philip Torsney, and Robert Weiss.

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