

PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Stinging-Insect Hypersensitivity: A 20-Year Study of Immunologic Treatment

Harry Louis Mueller, William H. Schmid and Rosalinda Rubinsztain

Pediatrics 1975;55:530-533

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://www.pediatrics.org>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 1975 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



3. Hable, K. A., Logan, G. B., and Washington, J. A.: Three *Hemophilus* species. *Amer. J. Dis. Child.*, 121:35, 1971.
4. Krishnaswami, R., Schwartz, J., and Boodish, W.: Pathogenicity of *H. parainfluenzae*. *Pediatrics*, 50:498, 1972.
5. Parker, R. H., and Hoeprich, P. D.: Disk method for rapid identification of *Hemophilus* species. *Amer. J. Clin. Path.*, 37:319, 1962.
6. Smith, E. S.: Purulent meningitis in infants and children. *J. Pediat.*, 45:425, 1954.
7. Bergstrand, C. G., Fahlén, T., and Thilén, A.: A follow-up study of children treated for acute purulent meningitis. *Acta Paediat.*, 46:10, 1957.
8. Vernon, M.: Meningitis and deafness: The problem, its physical, audiological, psychological, and educational manifestations in deaf children. *Laryngoscope*, 77:1856, 1967.
9. Schwartz, J. F.: Ataxia in bacterial meningitis. *Neurology*, 22:1071, 1972.
10. Yabek, S. M.: Meningococcal meningitis presenting as acute cerebellar ataxia. *Pediatrics*, 52:718, 1973.

ACKNOWLEDGEMENT

I would like to thank Doctors Richard Kesler, John Freeman, and David Carver, of the Johns Hopkins Hospital, and Doctor John B. Robbins of the National Institutes of Health for their suggestions. Miss Pat Rhine assisted.

Stinging-Insect Hypersensitivity: A 20-Year Study of Immunologic Treatment

Systemic hypersensitivity to stinging insects has been shown to be a life-endangering condition that can be treated by injections of insect extracts, resulting in protection against reactions to subsequent stings in a high percentage of treated patients.¹⁻³ The purpose of this study was to explore the effectiveness of the treatment and find indication for improving or refining it.

Previous published experience² had resulted in recommending that all patients having a systemic reaction to an insect sting should receive immunizing injections with aqueous whole-body insect extracts, first building up to a maintenance dose and then for a three-year period with increasing intervals between injections from once each month the first year, once every two months the second year, up to every three months the third year and with maintenance dosage as tolerated equal to the antigenicity of one or more average stings of each of the four hymenoptera—bee, wasp, hornet, and yellow jacket. Maintenance doses in these reported cases varied from 0.3 ml of 1:100 dilution to 0.2 ml of 1:10 dilution.

After a 20-year period of treating over 700 such patients on that regime, it became apparent that discontinuing immunotherapy after three years resulted in an occasional patient having a systemic reaction to subsequent stings. When two of these reactions became severe enough to be life-endangering, further study seemed indicated.

MATERIAL AND METHODS

All patients had been treated and followed by one author (H.M.) and for accurate data only the

400 patients that could be seen and interviewed were included in the study. Each patient had a complete original work-up with detailed records, and progress reports at intervals of six months or less for the three years of treatment.

Original systemic reactions were classified in four groups according to clinical severity of the symptoms as shown in Table I. Three weeks or more after the original systemic reaction, serial intracutaneous skin testing was done with extracts of whole-body bee, wasp, hornet, and yellow jacket.⁴ To interpret a test as positive an erythema of at least 2 cm in diameter with a wheal larger than that caused by the test injection and a negative control were required. All tests were checked at 24 and 48 hours for reappearance of erythema and induration indicating delayed hypersensitivity. The significance of this has been discussed in previous reports.^{4,5} Treatment was given with mixed whole-insect extract of equal parts of bee, wasp, hornet, and yellow jacket according to the above described plan. Data were recorded on IBM cards at the time of the interview and subjected to computer analysis.

RESULTS

Figures on sex and age range (Table II) of pediatric patients (0 to 19 years) were approximately the same as previously reported^{3,5} with 268 (67%) male and 132 (33%) female. The reason for the male preponderance is not known. Of these patients 319 (79%) were in the age group 0 to 19 years and these were divided into 45 (11%) under 5 years of age, 192 (48%) between 5 and 10 years, and 82 (21%) between 11 and 19 years. The reason for the preponderance of 5- to 10-year-olds is not known but the authors thought it might indicate a

TABLE I
CLASSIFICATION OF STINGING-INSECT SENSITIVITY

Grade	Signs and Symptoms
I. Slight general reaction	Generalized urticaria, itching, malaise, and anxiety
II. General reaction	Any of the above plus two or more of the following: generalized edema, constriction in chest, wheezing, abdominal pain, nausea and vomiting, and dizziness
III. Severe general reaction	Any of the above plus two or more of the following: dysphagia, hoarseness or thickened speech, confusion, and feeling of impending disaster
IV. Shock reaction	Any of the above plus two or more of the following: fall in blood pressure, collapse, incontinence, and unconsciousness

TABLE III
INTERVAL BETWEEN FIRST KNOWN STING AND REACTION STING

Interval (yr)	No.
1	77
2	36
3	27
4	13
5	11
6	5
7	7
9	5
10	3
11	3
12	1
13	2
16	2
17	1
18	1
24	2
25	1
28	1
33	1
35	3
38	1
42	1
44	1
46	1
48	1

TABLE II
PROFILE OF 400 PATIENTS

Data	No.	%
Sex		
Male	268	67
Female	132	33
Age (yr)		
0 to 4	45	11
5 to 10	192	48
11 to 19	82	20
Total pediatric	319	79
20+ (adult)	81	21
Family history of sting sensitivity	59	15

TABLE IV
TIME INTERVAL BEFORE REACTION

Time (min)	Total No.*	Grade of Reaction			
		I	II	III	IV
5	115	38	38	24	15
5 to 9	80	29	26	17	8
10 to 14	94	51	27	11	5
15 to 19	23	10	9	1	3
20 to 24	17	9	4	2	2
25 to 29	12	4	6	1	1
30 to 34	14	8	4	2	0
35	35	27	6	2	0
Total	390	176	120	60	34
No. & % with symptoms in less than 15 min		118 60%	91 75%	52 86%	28 88%

*No record of time interval could be obtained in ten patients.

TABLE V
REACTIONS TO STINGS

Reactions	No.	%
Increasing local reactions before systemic reactions	50	12
% of 50 patients with severe reactions		
Grade III	11	22
Grade IV	10	20
Total	21	42
% of all 400 patients with severe reactions		
Grade III	60	15
Grade IV	34	8.5
Total	94	23.5

TABLE VI
SYSTEMIC REACTIONS DURING AND AFTER TREATMENT

	No. Stung	No. With Systemic Reaction	%	Grade of Reaction			
				I	II	III	IV
During treatment	217	11	5	10	1	0	0
After treatment	108	7	6	3	1	3	0
On maintenance dose of <0.1 ml of 1:10 dilution	107	12	11	8	2	2	0
>0.1 ml of 1:10 dilution	218	6	3	5	0	1	0

greater tendency to exposure at this active, inquisitive age. A surprising figure was the number of patients, 59 or 15%, who gave a family history of what presumably were systemic reactions to stinging insects. The family relationships were restricted to siblings, parents, aunts, uncles, and grandparents. There is no known clinical significance.

Serial intracutaneous testing was of value in determining the approximate degree of skin sensitivity to the testing extract at the time and the dose dilution that could be used safely to start treatment without constitutional reaction and with the elimination of unnecessary inoculations. All patients were started on treatment with the dilution that gave the initial positive test and no patients had any constitutional reaction with the starting dose. No apparent long-term harmful side effects have resulted from the treatment during the period of observation. Occasional uncomfortable local reactions and rare immediate systemic reactions have followed therapeutic injections. Similar lack of apparent side effects has been reported in 2,606 cases followed elsewhere.³

Where known, in 207 patients, shown in Table III, the interval between the first known sting and the reaction causing sting was five years or less in 164 or 80%, with the remaining 20% scattered over intervals of 6 to 48 years. This suggests that if a patient is going to develop stinging insect sensitivity it will develop within a few years after the first sting.

Skin reactivity by testing parallels clinical sensitivity in most cases, but two patients with severe reactions had no demonstrable skin sensitivity. The authors believe that this suggests that sting reactions may be on a nonimmunologic basis. Because of the life-endangering possibility with sting reactions and our inability to prove these were not immunologic, it was considered justifiable to

give these two patients immunologic treatment. Neither of them have been stung since receiving treatment.

In 390 patients where the time from sting to onset of systemic symptoms was known, this was correlated with the severity of the reaction in Table IV. It seems clear that a large percentage of the reactions occur within 15 minutes and the more severe the reaction, the higher that percentage.

There were 50 patients or 12% who gave a history of increasing severity of local reactions to stings, preceding the sting causing the first systemic reaction. Table V shows that the systemic reaction was severe grade III or IV in 21 or 42% of this group, while only 94 or 23.5% of the entire 400 had similar severe grade III or IV reactions. Local reactions, regardless of severity, had previously not been considered an indication for immunotherapy, but these figures suggest that if a patient is having increasingly severe local reactions with subsequent stings and then develops a systemic reaction to a sting, there is a much greater possibility that a severe life-endangering reaction will occur. It seems reasonable, therefore, to do serial intracutaneous testing in patients with that history and to consider the justification for specific treatment if those tests show positive skin reactions at 1:1,000 dilution or above.

Patients having systemic reactions during and after treatment are tabulated in Table VI. Of 217 patients stung during treatment, 11 (5%) had a systemic reaction, and of 108 patients stung after three years of treatment, 5 or (6%) had a systemic reaction. However, when these are correlated with the maintenance dose, 11% of those stung while on a maintenance dose of less than 0.1 ml of 1:10 dilution had systemic reactions, while only 3% of those stung while on a maintenance dose of more than 0.1 ml of 1:10 dilution had systemic

reactions. These figures seem to indicate that those patients on larger maintenance doses have greater protection.

The lapse of time between the end of the three-year treatment and subsequent stings with systemic reaction ranged from 3 to 96 months with no correlation or preponderance in any time period. Patients that had multiple simultaneous stings during or after treatment developed systemic reactions three times as frequently as patients with single-sting episodes.

CONCLUSIONS

It is evident that the degree of severity of the sting reactions and the degree of protectiveness from immunotherapy are dose-related. Immunologic treatment for three years seems to provide a high degree of protection⁶ but 5% of the patients did not have complete protection during treatment and an additional 5% of patients had a decrease in protection after treatment was stopped. Until a method is developed for determining whether clinical protection is present and persisting after three years of injection treatment, all patients should probably have some plan of continuing immunological treatment. As indicated in previous publications, one author's (H.L.M.) experience with patients relying on sting avoidance and emergency self-treatment for protection has proven to be disastrous in three cases and fatal in one instance. Some stinging insect reactions are probably not immunologic.⁶ Increasingly severe

local reactions to successive stings may be reason for considering immunologic treatment, depending on the circumstances in each case.

HARRY LOUIS MUELLER, M.D.

WILLIAM H. SCHMID, M.D.

ROSALINDA RUBINSZTAIN, M.D.

Division of Allergy, Children's Hospital
Medical Center, and

Department of Pediatrics, Harvard
Medical School

Boston, Massachusetts 02115

Read before the annual meeting of the American Academy of Pediatrics, October 15, 1972.

ADDRESS FOR REPRINTS: (H.L.M.) Division of Allergy, Children's Hospital Medical Center, 300 Longwood Avenue, Boston, Massachusetts 02115.

REFERENCES

1. Mueller, H. L.: Diagnosis and treatment of insect sensitivity. *J. Asthma Res.*, 3:331, 1966.
2. Mueller, H. L.: Insect allergy. In, Samter, M. (ed.): *Insect Allergy in Immunological Diseases*, ed. 2. Boston: Little, Brown & Co., chap. 51, 1971.
3. Insect Allergy Committee of the American Academy of Allergy: Insect-sting allergy: Questionnaire study of 2,606 cases. *JAMA*, 193:115-120, 1965.
4. Mueller, H. L.: Serial intracutaneous testing for bee and wasp sensitivity. *J. Allergy*, 30:123, 1959.
5. Mueller, H. L.: Further experiences with severe allergic reactions to insect stings. *N. Engl. J. Med.*, 261:374, 1959.
6. Reisman, R. E.: Stinging insect allergy-treatment failures. *J. Allergy Clin. Immunol.*, 52:257, 1973.

The Risks of Paracervical Anesthesia: Intoxication and Neurological Injury of the Newborn

Obstetrical pain during routine vaginal delivery has prompted many therapeutic approaches over the decades with agents gaining and losing favor. The risks of local anesthesia have seemed negligible and mishaps have seemingly been rare. Teramo and Widholm remarked in 1967 that paracervical block had become the most popular method of relieving obstetric pain during the first stage of labor over most of the world.¹ It is now an even more popular choice in large and small hospitals in the United States, and the fact that it can

be administered without an anesthetist by the obstetrician is certainly contributory.

The safety of local anesthetics in routine vaginal deliveries was questioned in a number of articles published between 1963 and 1968 describing paracervical block and epidural routes using several agents.²⁻⁵ Fetal deaths and morbidity were recorded, and the use of exchange transfusion to remove the local anesthetic agent from the newborn was suggested.^{6,7} Refinements of technique and dosage for paracervical and epidural anesthesia were proposed to minimize risk.^{1,8,10}

Little is known about the frequency and recognition of local anesthetic mishap in routine obstetrics and less still about the fate of survivors. It is the purpose of this communication to describe the intoxication of a newborn by mepivacaine anesthesia and his survival and neurological abnormalities at 4 $\frac{1}{2}$ years.

Stinging-Insect Hypersensitivity: A 20-Year Study of Immunologic Treatment

Harry Louis Mueller, William H. Schmid and Rosalinda Rubinsztain

Pediatrics 1975;55:530-533

Updated Information & Services

including high-resolution figures, can be found at:

<http://www.pediatrics.org>

Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:

<http://www.pediatrics.org/misc/Permissions.shtml>

Reprints

Information about ordering reprints can be found online:

<http://www.pediatrics.org/misc/reprints.shtml>

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

