

Prolonged interval hyposensitization therapy in Hymenoptera-sensitive patients

**Monroe Coleman, M.D., James H. Barnard, M.D., Solomon E. Barr, M.D.,
Halla Brown, M.D., Macy I. Levine, M.D., and Harry L. Mueller, M.D.**
Stamford, Conn.

The Committee on Insects of the American Academy of Allergy has conducted a 10-year study of 397 patients with Hymenoptera allergy treated with glycerosaline or aqueous whole body mixed Hymenoptera extracts at intervals of 2 or 3 months for the maintenance doses. Patients had few reactions, although in some cases local reactions prevented lengthening of the interval. The clinical response was similar to that from conventional therapy using the 4-wk interval for maintenance doses. This type of therapy offers the added advantages of fewer patient visits and decreased cost.

In treating Hymenoptera-sensitive patients by conventional immunotherapy with whole body extracts, maintenance doses are usually given every 4 wk. Following the observation that such doses could be tolerated at 2-mo intervals or longer with excellent protection,¹ the Committee on Insects of the American Academy of Allergy conducted a 10-yr study to evaluate the efficacy and safety of administration of maintenance doses at prolonged intervals. Such therapy offers the advantages of greatly reduced cost and inconvenience to the patient, allowing for greater acceptance of a form of treatment that may be prolonged or indefinite.

The 397 patients in this study were obtained from the private practice of the authors.* Immunization was accomplished by giving injections of standard commercial glycerosaline or aqueous whole body extracts, containing equal parts of bee, hornet, wasp, and yellow jacket extracts, at approximately weekly intervals until a maintenance dose was reached. The latter represented the highest dose that each patient could tolerate comfortably. It was desirable to reach a dose between 0.2 ml and 0.5 ml of the 1:10 concentration of extract. However, some patients could not reach this level because of the development of local swellings with lower dosages. When the maintenance dose was determined, the interval was increased gradually to 4 wk and maintained for approximately 1 yr. The interval was then gradually increased 1 wk at a time until an 8-wk interval was reached. One investigator (HLM) proceeded directly from a 1-mo to a 2-mo interval. The patients continued the 8-wk interval during the second year of therapy. Then the interval was again increased by weekly increments

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Reprint requests to: Dr. Monroe Coleman, 144 Morgan St., Stamford, Conn. 06905.

*Cases were also contributed by Dr. Howard E. Voss.

TABLE I. Results of stings among 397 patients on or having completed prolonged interval hyposensitization

Interval	Number of sting episodes	Better	Same	Worse	Unknown*
2 mo	109	95 (97%)	3	0	11
3 mo	120	109 (98%)	1	1	9
Completed therapy†	21	16 (89%)	1	1	3
Total	250	220	5	2	23

*Received drug therapy as a precaution despite lack of symptoms.

†55 patients.

until a 12-wk interval was attained. The 12-wk interval was maintained for 1 yr or longer according to the clinical judgment of the physician. Some patients maintained a 2-mo interval for several years because of local reactions following injections. However, almost all were able to reach a 3-mo interval. Some patients were discharged after 3 yr of therapy and were observed for their response to subsequent stings.

There were 17 patients who could not tolerate an interval greater than 4 wk and, therefore, were not admitted to the study. They developed unusually large local reactions or, in rare cases, urticaria, as did 22 patients in the study whose interval could not be extended beyond 8 wk. None developed any severe reactions, and the remaining patients tolerated the procedure without difficulty. Up to this time, 135 patients are receiving treatment every 2 mo, and 207 are receiving treatment every 3 mo, while 55 have completed the 3-yr program and are being observed.

There were 278 males and 119 females in the study. Their ages ranged from under 5 to over 60 years of age with an approximately even distribution in the age groups under 12, 13-40 yr, and over 40 yr. The majority of patients developed symptoms within 30 min following a sting. Specifically, 110 patients developed reactions less than 5 min after the sting, 106 patients between 6 and 29 min, and 41 patients between 30 and 60 min after the sting. In addition, 27 patients developed reactions after 1 hr, and 4 patients developed reactions after 2 days. The interval was not clearly reported in 12 patients. Information was not available for the remaining patients.

Of the 397 patients studied, 134 had slight general reactions (generalized urticaria), 138 had moderate general reactions (urticaria, angioedema, chest constriction, wheezing, gastrointestinal symptoms, and dizziness), 62 had severe general reactions (the above symptoms plus dysphagia, hoarseness, dyspnea, confusion, and a feeling of impending disaster), and 40 had shock reactions (lowered blood pressure, collapse, and unconsciousness). There were 23 patients with unusually large local reactions.

The insect responsible for the reaction was reported to be a bee in 39 cases, hornet in 14 cases, wasp in 27 cases, and yellow jacket in 120 cases. In 131 cases the insect could not be identified. In the remaining 66 cases the identity of the insect was not recorded. Since many patients cannot identify the insect with certainty, it is difficult to evaluate such identification information.

TABLE II. Results of stings among 397 patients on or having completed prolonged interval hyposensitization classified as to severity of pretreatment reaction

Original sting reaction	Number of patients	Number of sting episodes	Better	Same	Worse	Unknown*
Shock	40	19	15			4
Severe general	62	46	39	1		6
Moderate general	138	71	65	1	1	4
Slight general	134	95	83	2	1	9
Local	23	19	18	1		
Total	397	250	220	5	2	23

*Received drug therapy as a precaution despite lack of symptoms.

RESULTS

The reactions of treated patients following subsequent stings were compared to the pretreatment reactions and were recorded as better, same, or worse. Those patients whose reaction was classified as better had, with rare exception, a mild local reaction without systemic effects. If, following a sting, the patient received any type of drug therapy as a precautionary measure, the response was listed as unknown. None of the 23 patients who elected to take such therapy had symptoms prior to or subsequent to the administration of these drugs. These patients were excluded from the statistical analysis of response to sting challenge.

There were 109 sting episodes among patients on the 2-mo interval: 95 were better (97%), 3 were the same, none were worse, and 11 were unknown. Of 120 sting episodes involving patients on a 3-mo interval, 109 were better (98%), 1 was the same, 1 was worse, and 9 were unknown. Fifty-five patients completed a 3-yr program, having been treated at a 3-mo interval for at least 1 yr. Of 21 subsequent stings in this group, 16 were better (89%), 1 was the same, 1 was worse, and 3 were unknown. Of the 2 treatment failures, one reaction occurred 3 yr and the other 5 yr after completing treatment (Table I).

Among the 40 patients who had shock reactions before treatment, 19 were stung again, all of whom were better, although 4 patients received precautionary medication. One patient, who collapsed several minutes after a pretreatment sting, developed a moderate general reaction following a subsequent sting while on treatment. He had ample time to get to his physician without difficulty. Either large or mild local reactions occurred in 14 patients.

Of 62 patients who developed severe general reactions prior to treatment, there were 46 subsequent stings, with 39 feeling better, 1 the same, and none worse, with 6 unknown. Of the 138 patients with moderate general reactions, there were 71 subsequent stings with 65 classified as better, 1 the same, 1 worse, and 4 unknown. In the 134 patients with slight general reactions, 95 stings occurred again and 83 were classified as better, 2 the same, 1 worse, and 9 unknown. Of 23 patients with large local reactions, there were 19 re-stings with 18 classified as better and 1 the same.

There were only 2 cases in this entire series of 250 sting episodes that were worse following treatment. One patient progressed from a slight general reaction

to a moderate general reaction, and the other from a moderate to severe general reaction (Table II).

DISCUSSION

Over a 10-yr period, 397 patients with Hymenoptera sensitivity have been treated with glycerosaline or aqueous mixed whole body Hymenoptera extracts, the maintenance dose being given every 4 wk during the first year, every 8 wk during the second year, and every 12 wk during the third year. The reactions of patients to subsequent stings during or following the treatment program were compared with reactions to stings prior to treatment. Of 209 sting episodes that could be evaluated during the prolonged interval therapy, 204 (97.5%) were better than prior to therapy, 5 were the same, and 2 were worse. The response of the patients on the prolonged interval therapy was similar to that in patients receiving maintenance doses at monthly intervals.^{2, 3, 4} Treatment was well tolerated without constitutional reactions, except in a few instances. Local swellings did occur and interfered with prolongation of the treatment in some cases. The advantages of prolonged interval therapy were its greater convenience, decreased cost, and equal effectiveness as compared with conventional therapy. Also, since it is not known at present when treatment can be safely discontinued, a booster series type of therapy is much more readily accepted by patients, with fewer dropouts than the conventional monthly injection for an indefinite time.

The present study is being extended to include patients receiving maintenance doses at 4, 5, and 6-mo intervals. The results to date are encouraging. Insect allergy may be unique in allowing treatment to be administered with glycerosaline or aqueous extracts at intervals considerably beyond the usual 4 wk. Perhaps this indicates that true desensitization may have occurred. It is hoped that this study might stimulate research to determine which patients need treatment, when such therapy may be safely terminated, and how to select that small number of potential treatment failures with whole body extracts who may benefit from venom therapy.

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