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Maintenance of Protection in Patients Treated for Stinging Insect Hypersensitivity: A Booster Injection Program

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Pediatrics 1977;59:773-777

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American Academy of Pediatrics

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valuable for the prenatal detection of congenital nephrosis in populations at risk, e.g., Finland, an elevated AFP concentration leading to amniotic fluid AFP studies. However, exclusion of congenital nephrosis by serum assay alone is clearly not possible. Hence, women at risk for having affected children should rather be offered amniotic fluid AFP studies as the most reliable method of prenatal detection.

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Supported in part by grants HD09281, HD05515, GM07015, and AM18729.

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ACKNOWLEDGMENT

We thank Dr. Nicholas Starkovsky of Princeton Laboratories for radiolabeled reagents for the AFP assay; Dr. Morris J. Karnovsky for advice in the interpretation of the electron micrographs; and Richard Amato, Clara Trummer, Ellen Morgan, and Justine and Bernard Collins for technical assistance.

Maintenance of Protection in Patients Treated for Stinging Insect Hypersensitivity: A Booster Injection Program

Previously reported studies of hypersensitivity to stinging insects have indicated that the antigens in the venom are present in the whole

body of the insects. Titration with weight-by-volume serial dilutions of whole body extracts against venom extracts in vivo by intracutaneous testing on clinically sensitive patients has shown that 0.05 ml of a 1:10 dilution of whole body extract had the approximate antigenic equivalent of 0.005 ml of venom.¹ This was confirmed by O'Connor and Erickson² with in vitro comparison studies.

With currently available methods, I do not believe it is possible to produce venom extracts of each of the four Hymenoptera in quantity to supply the needs for testing and treatment at a cost that would be within the reach of most patients. Yet all of these patients must be protected now.

It is virtually impossible to obtain unchanged fresh venom from dissected venom sacs, even when quick frozen.²⁻⁵ Electrical stimulation of the insects is the only satisfactory method of collecting pure venom. This can be done individually in an apparatus described by O'Connor et al.,⁶ which they reported to be slow and tedious, obtaining pure venom from 15 to 20 insects per hour. Or it can be done on a platform of nylon with wires that is inserted in a bee hive; this causes the insects to sting and discharge venom through the nylon sheet to be collected on the underside. Currently, this method is feasible only with captive bees. In my experience with more than a thousand patients who had stinging insect hypersensitivity, reliably identified bee-stung patients constituted only 8% of my Hymenoptera-sensitive patients. Most patients with stinging insect sensitivity have cross sensitivities to one or more other species; this was indicated both by skin tests and clinical experience with reactions. These patients must be protected from the insect that caused the sting reaction and from the other Hymenoptera. Except in the case of bee keepers, identification of the stinging insect by the patient is rarely accurate and not reliable.^{1,4}

Many investigators and the report of the Insect Allergy Committee of the Academy of Allergy have reported 80% to 95% protection or improvement with subsequent stings in Hymenoptera-sensitive patients who were treated with whole body extracts. The initial paper on the subject was by Braun⁷ in 1925 and most recently a 20-year follow-up study was done on 400 patients.⁸ This is certainly a highly effective treatment of a potentially fatal condition, and there has been no report, to my knowledge, of any long-term undesirable or serious side effects from the treatment.

It has been reported^{4,8,9} that there are a small

number of patients who are not completely, or in some instances not even partially, protected by treatment with the usual dosage of whole body extract. Three such patients in my studies had systemic reactions to subsequent stings. They were protected from more subsequent stings when they were given a larger than usual dosage. Lichtenstein et al.¹⁰ have reported one individual with hypersensitivity to bees who was not protected by treatment with whole body extract at a dose of 4,000 protein nitrogen units per week. The source of the extract was not stated. Since the recommended minimum maintenance dose⁸ in whole body extract treatment is more than three times greater, it is not surprising that the dose might fail to protect in some cases. Based on that report of one case, headlines in *Medical World News*¹¹ and various lay publications proclaimed that allergists find venom treatment "vastly superior."

Venom as a source of treatment antigen was naturally the first consideration in my studies more than 25 years ago, but a satisfactory, economically feasible source of venom, particularly for the various wasps, was never found. As stated by Reisman¹² in the editorial report of the Insect Allergy Committee, "Immunity, generally thought to be a function of production of gamma G type blocking antibodies and/or lowering of the titer of gamma E antibodies, still cannot be measured in a reliable manner."

It is fortunate that we have investigators who are continuing precise immunological studies to find the answers to the many unsolved problems in insect allergy. It is unfortunate that sweeping conclusions based on one case should be used to attempt to deny the validity of years of investigation with thousands of patients by many investigators. When there have been hundreds or thousands of patients treated with venom, perhaps results will show that it is really superior to whole body extract treatment. Perhaps we will find there are still treatment failures. My first treatment failure on the resting of a treated patient occurred with the 72nd resting episode in the 52nd patient.

In a 20-year follow-up of 400 patients⁸ who had three years of immunological treatment with whole body extract on maintenance dosage of at least the equivalent of one or more stings, 6% had systemic symptoms of some degree when they were restung.

When these patients were separated by size of maintenance dose, the failure rate dropped to 3% in those with the larger doses. There is no question that the success of immunological treat-

TABLE I
HYMENOPTERA STING REACTIONS

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

ment in hypersensitivity states is dose related. Patients who had multiple simultaneous stings during or after treatment developed systemic reactions three times as frequently as patients with single-sting episodes; this, too, is an indication that the response of the patient to the allergen is also dose related.

MATERIALS AND METHODS

The original 400 patients in the 20-year follow-up study* and subsequent patients who completed three years of treatment by 1970 were told the statistical results of treatment and were offered two alternatives: either stop treatment and report once a year, or continue on an annual booster program, receiving an injection of their full maintenance dose of mixed bee, wasp, hornet, and yellow-jacket whole body extract (Hollister-Stier) each spring.

One hundred thirty-three patients have been on the booster program for four years. Eighteen of these have missed once and seven have missed twice. Two were stung in the year they missed, and neither one had any reaction to the sting. Detailed circumstances of each sting episode were recorded.

To establish the degree of severity of the sting reactions, all patients in all studies for 25 years were classified into four grades of severity from mild symptoms to shock reactions (Table I).

The original sting reactions of the 133 patients in the booster program fell into the grades shown in Table II.

RESULTS

Fifty-five of the 133 patients (41%) were restung with a total of 71 sting episodes; stings varied from single to multiple (Table III). This is a very high percentage of restings in a four-year period; there is no explanation. Patients were not encouraged to avoid exposure and even were chided for "not trying" in years when they returned without having been stung.

Maintenance doses in the 133 patients were 0.1 to 0.3 ml of a 1:10 dilution (Table IV).

There were mild urticarial systemic symptoms in two patients after resting episodes. Five of the 133 patients had local reactions of silver dollar size.

Of the two patients who had some evidence of slight systemic reaction after a sting, both (on a maintenance dose of 0.15 ml of 1:10 dilution) had

TABLE II
ORIGINAL STING REACTIONS

<i>Severity of pretreatment Sting Reaction</i>	<i>133 Booster Patients</i>	<i>55 Patients Restung</i>
Grade I	60 (45%)	27 (49%)
Grade II	34 (26%)	17 (31%)
Grade III	28 (21%)	9 (16%)
Grade IV	11 (8%)	2 (4%)

TABLE III
FIFTY-FIVE PATIENTS RESTUNG WITH 71 STING EPISODES

<i>Episodes</i>	<i>No.</i>
Single-sting	50
Two-sting	10
Three-sting	7
Multiple-sting	4
Total	71

TABLE IV
MAINTENANCE DOSES

Mixed Stinging Insect Extract* (ml)	133 Booster Patients	55 Patients Restung	Systemic Reaction
0.1	20	14	0
0.15	21	9	2
0.2	56	13	0
0.25	30	15	0
0.3	6	4	0

*1:10 dilution.

mild scattered hives with itching within 30 minutes of single-sting episodes in 1972. The first patient with hives after resting was the 33rd sting episode in the 26th patient stung. One of them, after the maintenance dose was increased to 0.25 ml, had a two-sting episode in 1973 without reaction. That patient gets a silver dollar-sized local reaction to the booster injection. A third patient reported a feeling of tightness in the throat five minutes after a multiple-sting episode. The "feeling" subsided in 15 minutes without medication and without any other symptoms. That patient gets a silver dollar-sized local reaction to the booster injection at a dose of 0.15 ml of one to ten dilution and is apprehensive about stings. We do not believe that this was a systemic reaction.

No patient who received a booster dose of 0.2 ml of 1:10 dilution or greater had any systemic symptoms with single- or multiple-sting episodes. My present recommended minimum maintenance dose for treatment and boosters is 0.2 ml of 1:10 dilution.

The sex distribution in the booster program was 82 males (62%) and 51 females (38%). Fifty-five of these patients were restung: 38 males (69%) and 17 females (31%). Compared with 400 patients with long-term follow-up, the percentages of sex incidence are quite similar throughout; males predominate about two to one.

Age range is slightly different than that in the previous study,⁶ with many more children than adults in the booster group. Of the 133 patients in the booster program, 102 (84%) were between the ages of 7 and 19 years and 31 (16%) were over the age of 19 years. Of the 55 patients who were restung, 47 (86%) were between 7 and 19 years old and 8 (14%) were over 19 years old. This increased percentage of children in the booster program suggests that parents are more con-

cerned about continuing treatment for their children than most adults are about protecting themselves.

SUMMARY

A program of annual booster injections of mixed stinging insect whole body extract was given to 133 patients who had previously had three years or more of immunological treatment for systemic reactions to Hymenoptera stings. Two patients who were restung had mild symptoms that were evidenced by a few scattered hives with itching. No patient on a dose of 0.2 ml of 1:10 dilution extract had any reaction when they were restung. It is believed, therefore, that this program merits continuation with that dosage for a period long enough to determine its true effectiveness. There is some indication that this is an improvement over the program which stops treatment after three years. There is further support for the belief that this condition and the treatment are dose related. There is also evidence for my belief that this sensitivity, and the treatment, differ from the usual atopic sensitivity in antibody-antigen response.

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Presented in response to receiving the Bret Ratnet Award in Pediatric Allergy at the annual meeting of the American Academy of Pediatrics in San Francisco, October 1974.

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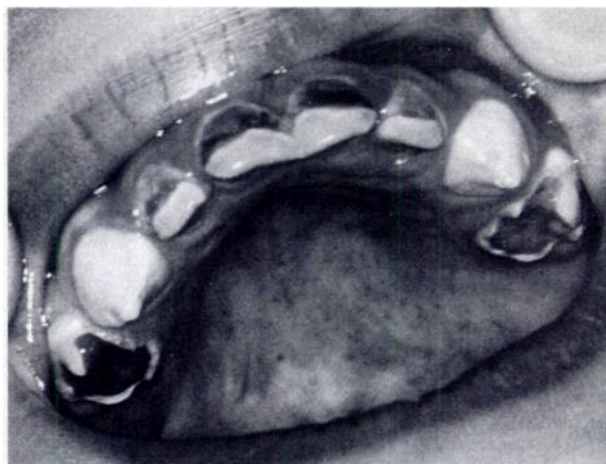


FIG. 1. Classical involvement of maxillary incisors and primary first molars.

Nursing Bottle Caries

Feeding habits affect dental health and ultimately the total health of young children. There is mounting concern among pediatric dentists about the increased incidence of nursing bottle caries in patients younger than 3 years old. Nursing bottle caries, nursing bottle syndrome, or bottle-propping caries are synonymous terms for a devastating condition that may render young children dental cripples. Typically, the primary maxillary incisors are affected most severely. The primary first molars are second in frequency; the most remarkable finding is that the mandibular incisors are seldom involved (Fig. 1 and 2). This is thought to be related to the protective effect of the tongue during suckling.

This type of rampant decay has been associated with prolonged bottle feeding beyond 12 months of age. History usually reveals that the child takes the bottle to bed at night and nap times. To relate this process to milk alone may be an inappropriate condemnation of a product that is nutritionally essential to the growth and welfare of the infant. The literature is not clear on this point and is quite controversial.¹⁻³ Animal studies suggest that lactose (a milk sugar) may enhance the implantation of cariogenic streptococci in the oral cavity.⁴ Furthermore, lactose can be metabolized

by plaque bacteria, resulting in potential acid demineralization of enamel.³ However, the cariogenic potential of milk supplemented with sucrose or the substitution of milk with beverages high in refined sugar content is beyond question. Sucrose is well known to facilitate implantation of cariogenic streptococci as well as to serve as an excellent substrate for acid production.⁵

The cariogenic potential of milk in nursing bottle caries probably reflects a situation of increased exposure time to a substrate which when conventionally consumed is of no harm. The decreased salivary flow rate during sleep renders the dentition more susceptible to acid production by plaque bacteria.⁶ These two factors, namely increased exposure time and decrease in salivary flow, seem to be critical in the etiology and pathogenesis of this condition.

Any child with nursing bottle caries should be referred to a pediatric dentist for evaluation. Because of the patient's young age and the extent of therapy that usually is necessary for reconstruction, ambulatory treatment in an office can rarely be performed. Rehabilitation usually requires hospitalization with provision of dental services in the operating room with the patient under general anesthesia.

In accordance with the problems associated with this disease process, the importance of prevention must be stressed. The following simple practices can help spare young children from this type of rampant caries:

1. When the parent is interviewed with regard to feeding habits, questions about nocturnal bottle habits should be asked.
2. Since nursing bottle caries is associated with prolonged nocturnal or nap time bottle usage,

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