

Letter to the Editor

Honeybee venom immunotherapy in children using a 50- μ g maintenance dose

To the Editor:

Venom immunotherapy (VIT) provides protection rates of between 80% and 97% from future systemic reactions. In children over a 10- to 20-year follow-up, VIT reduced the risk of future systemic reactions after an initial systemic reaction from 32% to 5%.¹

The recommended maintenance dose of VIT for adults and children is 100 μ g, which was initially chosen because it is double the venom content of an average venom sac (50 μ g).^{2,3} However, later studies documented a variable venom sac volume of up to 150 μ g.² For historical reasons, children younger than 14 years with venom anaphylaxis in Perth, Western Australia, received 50 μ g. The main advantage of using only 50 μ g in children is that a smaller injection volume is better tolerated with a lower cost. A previous study of both children and adults concluded that a 50- μ g dose might be sufficient for some patients after reporting systemic reactions in only 2.7% after VIT.² We retrospectively report on our experience with a 50- μ g honeybee venom maintenance dose in children.

This study identified 143 children who received VIT from either Princess Margaret Hospital for Children or Fremantle Hospital through a search of the Health Department of Western Australia database of patients admitted to the hospital between January 1987 and 2003 by using the International Classification of Diseases, Ninth and Tenth Revision, codes for "desensitization" and "anaphylaxis." Patients were excluded if they had a cutaneous reaction alone, did not receive a 50- μ g maintenance dose of VIT, did not complete at least 2 years of treatment, or had not completed their course more than 12 months before the study.

Medical records were used to establish initial honeybee sting reactions and doses of immunotherapy. Patients and families were contacted to confirm the initial reaction, duration of immunotherapy, and reaction after a subsequent field sting. All subjects who had a subsequent systemic reaction after completion of VIT were deemed not protected. This study had local institutional ethics approval.

Statistical analysis was performed with SPSS version 16.0 for windows (SPSS, Inc, Chicago, Ill). Continuous data were reported by using medians and interquartile ranges because of the nonnormal distribution of the data. A Fisher exact test was used for statistical comparison with previously published data, with a 2-sided *P* value of less than .05 being significant.

Of the 143 children identified, 110 were successfully contacted, and a further 25 were excluded, resulting in a response rate of 60%; 74% were male. The median age for commencement of VIT was 8 years (range, 2-14 years), duration of VIT was 3 years (range, 2-7 years), and the time since completion was 3.5 years (range, 1-17 years; interquartile range, 2.5-5.6 years).

During honeybee VIT, 34 subjects sustained 55 field stings with 7 mild-to-moderate systemic reactions. After completion of VIT, 44 subjects were stung 96 times (average of 2.2 stings per person stung), with 6 systemic reactions. All were of less severity than their initial reactions except one 8-year-old boy. He had

TABLE I. Comparisons of systemic reactions between Golden et al¹ and this study

Group	Contacted/eligible participants	No. stung (%)	Systemic reaction (%)
Golden et al ¹			
VIT	106/246	43 (41)	2 (5)
No VIT	46/99	22 (48)	7 (32)
Current study			
VIT	85/143	44 (51)	6 (13.6)*

**P* = .266 for VIT in the current study and the study by Golden et al.¹

angioedema and wheeze before VIT and then 3 episodes of systemic reactions requiring adrenaline during immunotherapy without a change in dose. After VIT was discontinued, he collapsed after a field sting and required adrenaline. His VIT should have been increased after the first systemic reaction to a field sting during VIT.

A 50- μ g maintenance dose prevented systemic reactions in 86.4% (38/44) of children for 93.8% (90/96) of stings after honeybee VIT. When a systemic reaction occurred, it was of lesser severity than the initial reaction in all but 1 child.

Compared with results published by Golden et al¹ using 100 μ g in children, there is no significant difference (Table I), although there is a trend toward higher protection rates with maintenance doses of 100 μ g (*P* = .266). Although this difference might be due to the dose, it should be noted that our children all underwent single VIT for honeybee venom allergy. Golden et al did not report the type of VIT administered, but previous studies from this group have contained predominantly (74%) participants with yellow jacket allergy.^{3,4} Yellow jacket VIT appears to be more effective than honeybee VIT,^{4,6} although the reason for this difference is not clear.⁶ Other studies containing children who received VIT are listed in Table II.^{1,2,5,7,8} Comparing our results with patients with honeybee venom allergy who received 100 μ g,^{5,7,8} the rates of protection with 50- μ g VIT for field stings appear similar. In the largest study there was a 14-year-old who, despite receiving a 100- μ g maintenance dose, had severe anaphylaxis to a subsequent sting that was similar to that seen in our child in whom treatment failed.

The immunologic and clinical effects of a maintenance dose of 50 μ g have previously been examined in 23 adults after 20 weeks of predominantly yellow jacket VIT with a reported 79% protection rate to challenge stings in those receiving 50 μ g compared with 96% protection in those receiving 100 μ g. The age of study participants is not documented. The 4 participants who were not protected experienced flushing, pruritus, or headache, all mild reactions not requiring treatment. On the basis of these results, they concluded that 50- μ g doses only offered partial protection, and the 50- μ g dose was not studied further; however, the treatment was for only 20 weeks, and there were immune responses to 50 μ g.^{2,3} Our study differs from other reported studies in that it involves a purely pediatric cohort who received honeybee VIT only.

This study is limited by reliance on the subjective reporting of reactions to stings, as in other studies. The participants were young children, and their recollections of reactions and duration

TABLE II. Protection from future systemic reactions after VIT

	Year published	No. of total patients receiving VIT	Age (y)	Stinging insect	Maintenance dose (μg)	Systemic reactions in those stung
Current study*	2010	85	2-15	Honeybee	50	13.6%
Golden et al ^{1†}	2004	106	Children	Not specified	100	5%
Reisman and Livingston ^{2‡}	1992	108	3-72	20% honeybee, 77% yellow jacket, 3% hornet	50	2.7%
Lerch and Müller ^{5§}	1998	120	11-70	Honeybee	100	15.6%
Müller et al ⁷	1991	86	10-62	Honeybee	100	17%
Urbanek et al ⁸	1985	29	4-20	Honeybee	100	7%

*Follow-up ranged from 1 to 17 years after completion of VIT.

†Follow-up ranged from 1 to 20 years after completion of VIT.

‡Data collected from 3 months to 8 years after starting VIT describe the 75 patients treated with single-venom VIT.

§Follow-up at least 3 years after completion of VIT.

||Follow-up 1 year after completion of VIT.

of VIT might be unreliable. Furthermore, the identification of the study population is not complete because no database existed for patients with honeybee venom allergy. We are aware that there were several years with no listings for desensitization admission when there should have been at least 30. Despite this, we believe that the respondents are representative of the population with bee venom allergy. Finally, our children received a standard 3 years of immunotherapy. It should be noted that we have not examined other factors predicting long-term protection, such as a longer duration of immunotherapy and reduction of venom-specific IgE levels over time.⁹

We conclude that honeybee VIT in children receiving a 50-μg maintenance dose prevents systemic reactions in 86.4% of children for 93.8% of stings, which is similar to the protection afforded by using a 100-μg maintenance dose of bee venom in adults.

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