

hospitals, whereas underdiagnosis of asthma can be expected in general populations.

Our results therefore suggest that subjects with T_{H1}-mediated autoimmune disease are less susceptible to T_{H2}-mediated disorders. We agree with Oro et al. that such findings may have far-reaching implications. Consequently, serum IgE levels should be determined in large samples of patients with MS and control subjects in order to further investigate this hypothesis.

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Reply

To the Editor:

We appreciate the interest of Dr. F. Neukirch et al. in our article "Regulation of disease susceptibility: decreased prevalence of IgE-mediated allergic disease in patients with multiple sclerosis (MS) (*J Allergy Clin Immunol* 1996;97:1402). It appears that they too have examined the epidemiology of asthma and allergies in patients with MS and have concluded, as we did, that allergic disease is less prevalent in patients with MS. Their patient population was much larger than ours and included more than 600 patients and more than 6000 control subjects, giving a great deal of strength to their study. However, the prevalence of allergy was determined in their study mainly by questionnaire. Studies based solely on questionnaire (and not also on the evaluation of allergen-specific IgE, which was included in our study) have difficulty in accurately identifying allergic individuals and have a tendency to overestimate (or underestimate, depending on the questions) the prevalence of allergy. Nevertheless, they have confirmed the results of our small pilot project, and we agree whole heartedly with their conclusions. We suggest though, that future studies in patients with MS include determination of allergen-specific IgE, rather than total serum IgE, as mentioned in their letter, to accurately assess for allergic disease.

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Discontinuing venom immunotherapy

To the Editor:

The article by Dr. Golden and colleagues entitled, "Discontinuing venom immunotherapy: outcome after five years" (*J Allergy Clin Immunol* 1996;97:579-87), is a significant addition

to our knowledge regarding the proper duration of venom immunotherapy. However, there appears to be an error in the Table I.

In year 4, zero of 24 patients in Group I and two of 24 patients in Group II had systemic reactions to challenge stings, giving a total of two of 48 patients. The total stings column notes that three of 96 stings resulted in a systemic reaction. A possible explanation for these data would be that a particular patient experienced systemic reactions to both of the sequential stings administered 1 month apart. However, the text notes that *none* (italics added) of the four patients who had reactions to the first sting reacted to the subsequent sting 1 month later.

Sequential stings 1 month apart were administered in year 4 in Groups I and II and in year 2 in Group III. Because reactions occurred in no Group I patients in year 4 and only one Group III patient in year 2, one may conclude that *three* Group II patients reacted in year 2. In order for the numbers to total correctly, one of these patients must have also reacted to the challenge sting in year 2. Furthermore, this proposal agrees with the data in Table II. Therefore it appears that Table I should be amended as follows:

Year	Group I	Group II	Group III	Total patients	Total stings
1	0/29			0/29	0/29
2	1/28	2/25	1/20	4/73	4/93
3	1/26			1/26	1/26
4	0/24	3/24		3/48	3/96
5	0/26			0/26	0/26
Total	2/29	4*/25	1/20	7*/74 (10%)	8/270 (3%)

*One of the patients in Group II reacted to challenge sting in both year 2 and year 4.

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Duration of venom immunotherapy

To the Editor:

The question of how long patients with stinging insect allergy should be treated by venom immunotherapy (VIT) is still unsettled. The recent publication by Golden et al. (*J Allergy Clin Immunol* 1996;97:579-87) gives valuable new information regarding this question. However, the conclusion of these authors, that VIT can be safely discontinued after 5 years in virtually all patients, needs some comments.

First, the excellent re-sting results 1 to 5 years after discontinuation of VIT with only 10% of 74 patients with mild systemic reactions during 270 sting challenges are in fact strong evidence in favor of their conclusion. However, these results were obtained in a vast majority of patients (at least 62 of the 74) who received VIT with mixed vespid venoms and half of them also with *Polistes* venom. These patients thus received a vespid venom maintenance dose of 300 to 400 µg per injection, whereas in most countries outside the United States, the maintenance dose is 100 µg. It is likely that short- and long-term results are more favorable with the much higher total dose given in the study by Golden et al. than with the 100 µg applied elsewhere. In fact, our re-sting results by field stings in 200 patients, 1 to 7 years after VIT, shown in Table I, point in this direction.

TABLE I. Results of field re-stings in 200 patients, 1 to 7 years after discontinuation of successful VIT

	Immunotherapy with	
	Bee venom	Vespa venom
No. re-stung	120	80
Mean duration of VIT in months (range)	56.3 (33-124)	52.8 (34-121)
No. of patients with systemic reactions (%) [*]	19 (15.8)	6 (7.5)
Systemic re-sting reaction during first year after VIT (%)	4 (3.3)	0 (0)
Later	15 (12.5)	6 (7.5)

^{*}Only 12 of 25 (48%) of the re-sting reactions were due to the first sting after stopping VIT.

Moreover, it must be stressed that the results found in patients almost exclusively allergic to vespids are not representative for patients allergic to honeybee stings. In these patients, the complete protection rate induced by VIT is only around 80%,¹ whereas it is above 95% in yellow jacket-sensitive individuals (*Vespa* spp.). Accordingly, the re-sting results after stopping VIT in patients allergic to honeybees are also less favorable than in patients allergic to vespids, as shown in Table I.

Our re-sting results, especially in patients allergic to honeybees, also indicate that the risk with increasing time after discontinuation of VIT is not decreasing, but rather increasing.

In summary, we think that more data on discontinuation of VIT in patients allergic to vespids with the 100 µg maintenance dose are needed and that long-term prognosis after stopping VIT in patients allergic to bees is less favorable than suggested by Golden et al.

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Reply

To the Editor:

Dr. Graft is quite astute in his observation and is correct in his analysis of the data depicted in Table I. In an early revision of the manuscript it was decided to change Table I from the way Dr. Graft shows it (above) to the format as published so that "the columns would add up." This was necessary because the reporting of "patients" (rather than "stings" as in the last column) was incremental, so that the patient who reacted for a second time in year 4 was not shown in those columns of the table because he was already included in the patient numbers for year 2. This method of display of the data is what created the discrepancy between the total stings in the last column and the patients in the other columns, as noticed by Dr. Graft. Table II does show that Patient 4 was indeed stung in year 2 and in year 4 and had mild systemic reactions both times.

Dr. Müller raises the very important point that observations made in patients allergic to yellow jackets do not necessarily apply to patients allergic to honeybees. However, this is not the same issue as the total venom dose. Dr. Müller's data, as shown, demonstrate a significant difference between honeybee and yellow jacket treatment, even though both groups received 100 µg maintenance doses. There have been previous reports that the maintenance dose of 100 µg of any single venom (yellow jacket, honeybee, or *Polistes* wasp) provides only an 80% to 85% rate of complete protection from allergic reaction to challenge sting, whereas 200 to 300 µg provides 95% protection.¹⁻³ The patients reported in our study were quite representative of our overall patient population: most patients receive mixed vespid venoms. It would have been appropriate for us to indicate in our discussion and conclusions that our findings cannot necessarily be extrapolated to patients allergic to honeybees nor to those treated with lower maintenance doses. We agree that additional data on such patients are needed.

On the question raised by Dr. Müller of risk with increasing time after discontinuation, our previous and current studies clearly report (like Dr. Müller) that no systemic reactions occurred in the first year after venom immunotherapy was discontinued,⁴ so in that sense the risk could be said to increase with time. However, it is not as clear that the risk increases (or decreases) more than 3 to 5 years after stopping therapy. Keating et al.⁵ reported that reactions occurred most often in the first year or two after therapy had been stopped. They also showed that the risk seemed to persist longer in those who had had only 1 to 3 years of therapy. We have noted that venom skin tests and specific IgE antibodies decrease steadily during the first 3 to 5 years after venom immunotherapy was discontinued with more and more patients having negative responses. This would certainly suggest that the risk should not increase after that point. There is a pressing need for more data on the long-term outcome; whether risk increases or decreases 5 to 10 years after stopping therapy cannot yet be concluded from our data or those presented by Dr. Müller. We look forward to future studies from Dr. Müller and other investigators in the field to elucidate the answers to these remaining problems.

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