

and the exact methods of insect handling and challenge procedures.

In all, we heartily agree with Franken et al. that a sting challenge may be used to establish the stinging insect responsible for anaphylaxis. We have reported, however, the lack of association between plasma levels of specific IgE or IgG, as well as skin test results and the occurrence and severity of anaphylaxis after sting challenge (J ALLERGY CLIN IMMUNOL 1994;94:151-9). Because Franken et al. have not demonstrated any IgE or IgG data in their article, we disagree with their conclusion that demonstrable levels of venom-specific IgE (or skin test reactivity) should be included as criteria for initiating venom immunotherapy.

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#### REFERENCE

1. Franken HH, Dubois AEJ, Minkema HJ, Van der Heide S, De Monchy JGR. Lack of reproducibility of a single negative sting challenge response in the assessment of anaphylactic risk in patients with suspected yellow jacket hypersensitivity. J ALLERGY CLIN IMMUNOL 1994;93:431-6.

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#### Analysis of insect-sting study

To the Editor:

The article by van der Linden et al. (J ALLERGY CLIN IMMUNOL 1994;94:151-9) presents a large amount of clinical data. I have two analytical questions about this study.

First, was the ratio between the RAST class and the log of the specific IgG examined as a possible factor? This is a logical transformation because one factor is positively associated and the other is negatively associated with recurrent reactions. Use of a ratio might show significance, even if each factor separately did not. A plot of this ratio against clinical sting challenge reactions would be helpful, at least to this reader.

Second, did logistic regression use broader groupings of interval data, such as subjects with clinical reactions greater than or equal to class II or class III as outcome variables? (There were relatively few subjects with these reaction classes.)

Also, the use of continuous or interval variables as independent variables without broader groupings sometimes results in too many strata to build reliable prediction models. A goodness-of-fit test is a helpful way to

examine how well logistic regression models predict outcome.<sup>1</sup>

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#### Reply

To the Editor:

Dr. Lin makes two constructive comments. First, the ratio of IgE and IgG might indeed have a predictive value for the clinical severity of an anaphylactic reaction. Unfortunately, such a relation was nonexistent in our patients. Second, broader grouping of clinically stratified patients might show more predictive power. Because of this argument, we have already combined the two potentially life-threatening grades of anaphylactic reactions (grades III and IV, i.e., pulmonary and cardiovascular symptoms). We have only observed relations as indicated in our article and do not think that the combinations of more clinical symptoms or the use of other statistical tests may be more informative.

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#### Insect-sting challenges—all risk and no benefit?

To the Editor:

The article regarding insect-sting challenge by van der Linden et al. (J ALLERGY CLIN IMMUNOL 1994;94:151-9) is certainly interesting, but I fail to see the benefits for our patients or our health care system, which Dr. Lichtenstein (J ALLERGY CLIN IMMUNOL 1994;94:137-8) predicts if the findings are confirmed.

My main concern regards the selection bias inherent in this study, because the article does not state the number of subjects that declined the sting challenge. Presumably, there were enrollable subjects, who had such severe sting reactions that they were afraid they might die during a sting challenge, and were willing to "take their chances" on not getting re-stung, rather than

be stung intentionally. This selection bias would artificially decrease the risk of sting challenge in the study.

I also disagree with the underlying assumption that sting challenge is safe just because none of the 324 subjects challenged had a severe reaction. Besides the selection bias, this assumption ignores the fact that, sooner or later, a subject will die during sting challenge. Even under the best of conditions, anaphylaxis can be fatal.<sup>1</sup> Whether the risk of death per sting challenge is 1 in 1000 or 1 in 10,000, it is hard to justify, especially because no deaths caused by venom immunotherapy have been reported.<sup>2,3</sup>

This type of challenge is not consistent with the treatment of other life-threatening conditions in the United States. We do not require patients to have a stroke before treating their hypertension, or a myocardial infarction before treating their hypercholesterolemia. We may be overtreating some of these conditions, but that is the nature of life-threatening diseases.

Finally, these sting challenges will cost more than the immunotherapy. Assuming \$25 per injection for the extract and administration, 4 years of immunotherapy would cost roughly \$1200. The intensive care unit admission, chest x-ray, electrocardiogram, and blood tests included in the study would usually cost at least \$1200 in the United States.

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## REFERENCES

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2. Reid MJ, Lockey RF, Turkeltaub PC, Platts-Mills TA. Survey of fatalities from skin testing and immunotherapy 1985-1989. *J ALLERGY CLIN IMMUNOL* 1993;92:6-15.
3. Lockey RF, Turkeltaub PC, Olive ES, et al. The Hymenoptera venom study. III. Safety of venom immunotherapy. *J ALLERGY CLIN IMMUNOL* 1990;86:775-80.

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## Sting challenges

### *To the Editor:*

The recent editorial on reappraisal of sting challenge as the decisive criterion for instituting immunotherapy in clinically sensitive patients (*J ALLERGY CLIN IMMUNOL* 1994;94:137-8) must be questioned. Dr. Lichtenstein's initial instinct to discontinue this procedure after obtaining a near fatal reaction was correct and reflects the ethical tradition of not doing harm to a patient. In addition, a negative sting challenge response does not mean that the patient will be protected from a second sting challenge. Lichtenstein has such patients, and so do others. Franken et al.<sup>1</sup> recently reported on 61 patients who were rechallenged after they had a negative sting

challenge response. Anaphylactic reactions, some very-severe, occurred in 21% of these patients. They concluded that a single sting challenge should *not* be used to select patients for immunotherapy.

I submit that we do not know enough about the natural history of insect sting allergy to determine what criteria should be used to institute immunotherapy, other than the clinical history or when to discontinue it in some patients. I am treating an 82-year-old woman, an avid gardener, who experienced severe shock after her third field sting by a yellow jacket. This occurred 5 years after completing a course of immunotherapy because of a similar reaction. She did not react after the other two prior stings. This experience has changed my approach to this problem. I believe we should consider treating all patients who have sustained life-threatening insect sting reactions indefinitely until more is known about when to stop. This is especially important in older patients with coronary artery disease who are prone to have a myocardial infarction associated with a sustained hypotensive reaction caused by a sting. I have had such a patient. Incidentally, it is very difficult to convince such patients to stop treatment; perhaps they know more than we do.

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## REFERENCE

1. Franken HH, Dubois AEJ, Minkema HJ, van der Heide S, de Monchy JGR. Lack of reproducibility of a single negative sting challenge response in the assessment of anaphylactic risk in patients with suspected yellow jacket hypersensitivity. *J ALLERGY CLIN IMMUNOL* 1994;93:431-45.

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## Serum eosinophilic cationic protein as a marker of disease activity in chronic asthma

### *To the Editor:*

We were interested to read the article by Ferguson et al. (*J ALLERGY CLIN IMMUNOL* 1995;95:23-8) investigating the role of eosinophil cationic protein (ECP) as a marker of disease activity in chronic asthma. The study failed to show any difference in serum ECP between patients with symptomatic asthma and those with asymptomatic asthma. The authors examined a measure of eosinophil activation derived from "number of cells (eosinophils) per microgram of ECP." There was a significant difference between activated eosinophils in the patients with symptomatic asthma and those in patients with asymptomatic asthma. ECP measurement reflects the ECP level in vivo (approximately 10%) and a major component released by the eosinophils during processing of the sample (90%). This occurs after degranulation of the eosinophils, which is triggered by contact with glass. The extent of degranulation is depen-