

Correspondence

Insect sting challenges: Do no harm

To the Editor:

Hippocrates initially counseled physicians, above all, "do no harm." Any intentional diagnostic procedure that can cause symptoms or distress, particularly reactions as severe as anaphylaxis, must be ethically and medically justified. The use of the intentional sting challenge as a diagnostic tool to determine the need for venom immunotherapy in patients with prior sting anaphylaxis is a prime example. In my opinion, the risks and suggested benefits do not justify the intentional sting challenge as a diagnostic procedure.¹

Studies of the natural history of insect sting allergy have persistently shown the dichotomy between immunologic reactivity and clinical sensitivity. Only about 60% of individuals with a history of anaphylaxis and positive venom skin test results react when re-stung. Reactions are more likely to recur in adults and in individuals of any age who have had more severe anaphylaxis. The use of intentional sting challenges as a means of improving the clinical efficacy of current diagnostic procedures for selection of patients for venom immunotherapy was evaluated in the past^{2,3} and recently reassessed in the Netherlands.⁴

In their most recent article (*J ALLERGY CLIN IMMUNOL* 1994;94:151-9), van der Linden et al. report that only 25% of yellow jacket-sensitive and 52% of honeybee-sensitive patients reacted to a sting challenge. Patients all had a history of sting anaphylaxis and varying degrees of skin test reactivity. They were tested with 0.1 ml volumes of insect venoms, about four times the usual normal volume. Without control data, it is hard to interpret the significance of these skin tests, and thus there may have been patients who would not normally qualify for immunotherapy on the basis of our current standards. Thus these re-sting reaction rates may be skewed to a lower incidence.

The first question is the validity of a single sting challenge. In another study from the Netherlands, Franken et al.⁵ reported that 21% of patients who tolerated a first challenge had a systemic reaction after a second challenge. In our studies of the natural history of insect sting allergy,⁶ about 30% of patients had inconsistent responses, reaction or no reaction, to repeated re-stings. Thus the diagnostic credibility of the response to a single sting challenge is certainly suspect.

As for the ethical issue, severe reactions to sting challenges are perhaps best exemplified by the Johns Hopkins experience.⁷ van der Linden et al. reported that after challenge, 38 patients had severe anaphylaxis (grades 3 and 4 in their classification). In an earlier article van der Linden et al.⁴ reported that 17 patients required overnight observation in an intensive care unit. Franken et al.⁵ reported that six of 13 patients who reacted to challenges had severe symptoms.

Venom immunotherapy is most important for patients who have had severe anaphylactic symptoms. In this group, the re-sting reaction rates are high, with the likelihood of a recurrent similarly severe reaction.⁶ Immunotherapy may not be necessary for patients with milder reactions. Hopefully, some other diagnostic criteria, which better identify patients at continued risk for sting anaphylaxis who need venom immunotherapy, will be found.

In the editorial accompanying the van der Linden article (*J ALLERGY CLIN IMMUNOL* 1994;94:137-8), Dr. Lichtenstein supports the concept of intentional diagnostic sting challenges and recommends testing this hypothesis in the United States. I strongly oppose that proposal as medically unsound and ethically indefensible.

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Reply

To the Editor:

Both Dr. Reisman and Dr. Novey point out that the results of the study by van der Linden et al. (*J ALLERGY CLIN IMMUNOL* 1994;94:151-9) do not take into account the fact that a single sting is not fully diagnostic, because

a reaction may occur after a subsequent sting. I also made this point in my editorial, stating "these authors have not proven that patients who have a negative response to an in-hospital sting will not have a reaction during a subsequent field sting." I point out that, indeed, we have seen such patients.

Both Dr. Reisman and Dr. Novey refer to a study by Franken et al., which I missed. This study is, indeed, quite useful; but it needs to be confirmed because it involves only 13 reactions, five or six of which required treatment. It should be noted that my editorial did not endorse the approach of van der Linden et al., but suggested that their data were important enough to require further study.

Dr. Reisman's position in his letter was my own, until I looked at the new data presented by van der Linden et al. However, his moral indignation that the van der Linden approach is "ethically indefensible" is not useful. All diagnostic procedures, including skin tests, carry the risk of reaction. The fact that none of the 328 patients studied by van der Linden et al. had a more serious reaction than that which occurred with their field sting and that only 10% had any kind of serious reaction that required therapy is a result that must be considered very seriously. In these days when health care dollars are not adequate and when health care itself is clearly being rationed (which is, I believe, a fact that *should* raise serious ethical questions), I think we need to study the economic aspects of medical care. The results of the study by van der Linden et al., if proven, could reduce by up to 90% the number of patients who are subjected to the cost of venom immunotherapy. I continue to believe that these results require further study.

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Sting challenges as criteria for venom immunotherapy

To the Editor:

It is surprising that neither van der Linden et al. (J ALLERGY CLIN IMMUNOL 1994;94:151-9) nor Lawrence Lichtenstein (J ALLERGY CLIN IMMUNOL 1994;94:137-8), in their article and editorial respectively, referenced the study by Franken et al.¹ The latter found that a second challenge sting identified 21% of subjects with anaphylactic reactions who were nonreactors during their first challenge. Because there is no quantitation of venom contents in a sting challenge, it is understandable that re-stings will produce variable responses.

It is also puzzling that reference number 38 in the study by van der Linden et al., which contains Franken's statement that "a single test does not reliably distinguish patients requiring immunotherapy from those who do not," was cited only in regard to

standardization, a subject not broached in that letter to *The Lancet*.²

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Reply

To the Editor:

Franken et al.¹ indicate the existence of two opposing schools of thought on whom to treat with venom immunotherapy. Nobody disagrees, however, that venom immunotherapy is indicated to prevent a future anaphylactic reaction to a field sting in a person who has experienced a previous anaphylactic reaction to an insect sting. The prediction of such a field-sting reaction is the essential goal of the in-hospital challenge procedure.

We are therefore very interested in the authors' data on the occurrence or lack of occurrence of an anaphylactic reaction to a field sting in their 138 patients who had a negative response to yellow jacket challenge. This parameter is, in our opinion, the correct biologic end point of their study on the in-hospital challenge procedure. Under our care, only 4% of patients who had a negative response to challenge, which was initiated because of an anaphylactic reaction to a field sting, had mild anaphylactic symptoms after a consecutive field sting. The results of an updated questionnaire among untreated patients with a negative or mild reaction to a sting challenge test will be published shortly. In accordance with our data, Drs. Blaauw and Smithuis (personal communication) report a 7% to 9% chance of developing anaphylaxis after a field sting by a yellow jacket or honeybee in hundreds of patients who had a negative sting challenge response to the same insect species.

There are only a few published prospective studies on insect sting anaphylaxis. Thus it would be very interesting to be informed of some more details on the patients and methods in the study by Franken et al., such as: field-sting data, data on honeybee stings, a possible relation between the severity of the first field-sting reaction and the severity of the second sting challenge reaction, a possible relation between the interval between the two challenges and the severity of the second reaction, their definition and assessment of hypotension,