

REFERENCES

1. Adkinson NF. Side chain specific beta lactam allergy. *Clin Exp Allergy* 1991;20:445-7.
2. Audicana M, Bernaola G, Urrutia I, et al. Allergic reactions to betalactams: study in a group of patients allergic to penicillins and evaluation of cross-reactivity with cephalosporins. *Allergy* 1994;49:108-13.
3. Blanca M, Vega JM, Garcia J, et al. Allergy to amoxicillin with good tolerance to other penicillins. Study of the incidence in patients allergic to beta-lactams. *Clin Exp Allergy* 1991;20:475-81.
4. Blanca M, Mayorga C, Sanchez F, et al. Differences in serum IgE activity to benzyl penicillin and amoxicillin in sera from patients allergic to beta lactams. *Allergy* 1991;46: 632-6.
5. Mayorga C, Blanca M, Moscoso J, et al. Studies of the epitopes of amoxicillin by monoclonal antibodies. *Int Arch Allergy Appl Immunol* 1992;99:443-5.
6. Nagakura N, Souma S, Shimizu T, Yanagihara Y. Anti-ampicillin monoclonal antibodies and their cross-reactivities to various beta lactams. *J Antimicrob Chemother* 1991;28:357-68.
7. Terrados S, Vega JM, Blanca M, et al. Evaluation of delayed allergic reactions to penicillins [Abstract]. *J ALLERGY CLIN IMMUNOL* 1993;91:263.
8. Carson JL, Strom BL, Morse ML. Medicaid data bases. In: Strom BL, ed. *Pharmacoepidemiology*. New York: Churchill Livingstone, 1989:173-88.

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Intentional diagnostic sting challenges: an important medical issue

To the Editor:

In a letter in the May 1993 issue of the JOURNAL, Robert E. Reisman (page 1100) expresses his concern about three aspects of our study in which deliberate sting challenges were performed (*J ALLERGY CLIN IMMUNOL* 1992;90:110-8). First is the potential danger of inducing an anaphylactic reaction in otherwise healthy subjects. In the referred study by Smith et al. and in the original study on which this article was based,¹ no clinical data on any of the 59 insect-sting-challenged subjects were given. In three patients anaphylactic shock developed, but we were not informed about the use of β -blockers or concurrent atherosclerotic, pulmonary, or other diseases in these patients, which might have influenced the clinical reaction after the sting. In our study, subjects were selected carefully to minimize potential risks due to sting challenges. In addition, all challenges were carried out in an intensive care unit. When a severe anaphylactic reaction occurred (17 of 138 subjects), these persons stayed overnight for observation. As indicated, none of them required any additional therapy. There was thus no medical indication,

other than a need for reassurance, for keeping these subjects hospitalized.

The second concern of Dr. Reisman deals with the identification of subjects at risk of developing another insect-sting anaphylactic reaction. Fortunately, insect-sting anaphylaxis is a self-limiting disease in most persons.² We agree with Dr. Reisman that the severity of the previous reaction relates to some degree to the reaction after a future sting. However, in our view this is not a sufficient criterion for starting immunotherapy. In a recent article (*J ALLERGY CLIN IMMUNOL* 1994;94: 151-9), we describe 324 subjects with previous insect-sting anaphylaxis. Of these subjects, 48% of the honey-bee-sensitive persons and 75% of the yellow jacket-sensitive persons did not react at all to a sting challenge. Of the patients with a previous severe reaction, only 30% of honeybee-sensitive persons and 15% of yellow jacket-sensitive persons had a severe reaction after this sting challenge. Upgrading from mild to severe reactions was never observed. In addition, none of the tests to assess insect-sting hypersensitivity (i.e., skin test, IgE, IgG₄) significantly related to the reaction after sting challenge, as demonstrated previously.³ Alarmingly, approximately 5% of subjects with negative skin test results or undetectable plasma levels of specific IgE did have a second anaphylactic reaction after sting challenge. These patients would normally not have been treated with venom immunotherapy, but they were at risk for a severe anaphylactic reaction after a future field sting. However, we prospectively demonstrate that subjects with a mild reaction after a field sting may not need to be treated with immunotherapy at all, and in this respect we agree with Dr. Reisman.

The real concern of our sting-challenge procedure was the reaction after future field stings. Preliminary results from questionnaires sent to all our (untreated) subjects with a negative sting-challenge test result show approximately 4% recurrence of (mild) anaphylactic symptoms after a field sting up to 10 years after the challenge. This rate is comparable to the prevalence of insect-sting anaphylaxis in the general population.² This indicates a benefit of relieving approximately 80% of subjects from unnecessary, costly, and time-consuming immunotherapy versus a 4% risk for a mild anaphylactic reaction in untreated subjects. Although we are well aware of the potential legal consequences regarding the sting-challenge procedure in the United States, we think that this risk-to-benefit ratio is low enough to advocate the standardized, in-hospital procedure as the best selection criterion for venom immunotherapy.

The third concern of Dr. Reisman is that we did not use epinephrine for treatment of all anaphylactic reactions in the intensive care unit. There are no prospective clinical trials on the use of epinephrine or any other medication in the treatment of anaphylaxis. We know that the therapeutic regimen in an intensive care

unit is not applicable to field stings. In our recent article in the JOURNAL, 324 subjects who previously had insect-sting anaphylaxis underwent a sting challenge. Anaphylactic reactions were observed in 96 (28%) of them. In 27 of these subjects hypotension developed. Three of these 96 patients received standard doses of epinephrine and were noted to have cardiac arrhythmias immediately after this therapy. The remaining 95 of these patients did not receive epinephrine but instead received varying regimens of intravenous antihistaminic drug and, if necessary, plasma expander. All of them recovered quickly and uneventfully. It is known that epinephrine therapy in anaphylaxis has a somewhat increased risk of death.⁴ Therefore in a clinical setting, epinephrine may not necessarily be the therapy of choice. The appropriate treatment of the anaphylactic reaction needs to be studied in both clinical and field settings.

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REFERENCES

1. Hunt KJ, Valentine MD, Sobotka AK, et al. A controlled trial of immunotherapy in insect hypersensitivity. *N Engl J Med* 1978;299:157-61.
2. Lockey RF, Turkeltaub PC, Baird-Warren IA, et al. The Hymenoptera venom study I, 1979-1982: demographics and history-sting data. *J ALLERGY CLIN IMMUNOL* 1988;82:370-81.
3. Kampelmacher MJ, Van der Zwan JC. Provocation test with a living insect as a diagnostic tool for systemic reactions to bee or wasp venom: a prospective study with emphasis on clinical aspects. *Clin Allergy* 1987;17:317-27.
4. Waldhausen E, Keser G, Marquardt B. Der Anaphylaktische Shock. *Anaesthesist* 1987;36:150-8.

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