exposed to thimerosal, it is more likely that her sensitization followed the previous administration of RhoGAM.

We believe our case is the first report of a delayed hypersensitivity reaction to thimerosal in $Rh_O(D)$ immunoglobulin. The case is instructive for a number of reasons. First, it illustrates the potential for significant delayed hypersensitivity reactions to a preservative in an immunologic product. As in any adverse drug reaction, care should be taken to examine all components of a product in order to identify the most likely responsible agent. Second, our evaluation was able to effectively dispel the initial assumption of the primary physician that the patient had experienced an immediate-type hypersensitivity reaction. We recognize, however, that a component of immediate hypersensitivity to RhoGAM was not absolutely ruled out because skin tests with this agent were refused by the patient. Finally, by demonstrating that thimerosal was the agent responsible for the delayed hypersensitivity reaction, an alternative lyophilized product was successfully administered, without adverse reaction, to prevent Rh isoimmunization.

REFERENCES

1. Grabenstein JD. ImmunoFacts: vaccines and immunologic drugs. 1st ed. St. Louis: Facts and Comparisons; 1995. p. 284-9.
2. Fisher AA. Contact dermatitis. 3rd ed. Philadelphia: Lea and Febiger; 1986. p. 178-81.
3. Noel I, Galloway A, Ive FA. Hypersensitivity to thimerosal in hepatitis B vaccine. Lancet 1991;338:705.
4. Rietschel RL, Adams RM. Reactions to thimerosal in hepatitis B vaccines. Dermatol Clin 1990;8:161-4.
5. Lohiya G. Asthma and urticaria after hepatitis B vaccination. West J Med 1987;147:341.
6. Maibach H. Acute laryngeal obstruction presumed secondary to thimerosal (merthiolate) delayed hypersensitivity. Contact Dermatitis 1975;1:221-2.
7. van't Veen AJ, van Joost T. Sensitization to thimerosal (merthiolate) is still present today. Contact Dermatitis 1994;31:293-8.

A simple device for deliberate Hymenoptera sting challenge

Arnon Goldberg, MD, and Ronit Confino-Cohen, MD *Kfar Saba and Tel-Aviv, Israel*

Deliberate insect sting challenge has been traditionally used to confirm protection from future stings in patients allergic to venom after they have undergone venom immunotherapy. The use of this method as an accurate diagnostic tool in highly selected patients was demonstrated.[1] Several European researchers have advocated using it as a diagnostic tool in the general venom-allergic population.[2] Although not used routinely in the United States, this approach gained some support on that side of the ocean as well.[3] Although deliberate sting challenge is a relatively simple procedure, most allergists have never performed it. None of the researchers performing it have described in detail how the challenge was carried out. Many variables may affect the outcome of a sting challenge, and the stinging technique may be one of them.

To facilitate the performance of sting challenges in clinical practice and to reduce one source of variability in their outcome, we developed a simple device with which we performed 62 successful deliberate stings with different hymenopterans. The device, which is basically a 50 ml disposable syringe, has proved to be safe and easy to use, and if it is accepted generally, the device may contribute to the standardization of the stinging technique.

METHODS

Fifty-nine patients (36 male and 23 female patients) aged 7 to 76 years (mean age, 33 years) were deliberately stung. All patients had experienced a systemic reaction after an insect sting in the past, and positive venom-specific IgE determination was obtained from each of them. Challenges were performed in three groups. In 32 patients currently receiving maintenance immunotherapy at 3-month intervals, challenges were performed to evaluate the safety and effectiveness of the prolonged interval protocol. In 23 patients challenges were performed 2 years after discontinuation of 3-year immunotherapy to evaluate the safety of this approach. In four patients in whom venom-specific IgE determination was not conclusive, challenges were performed for diagnostic purposes. Three patients were challenged twice with different insects, and the stings were performed 3 hours apart. The in-hospital sting challenges were performed with an insect of the species that had induced systemic symptoms in the past. The stinging insects included 39 honeybees, 20 yellow jackets, and three oriental wasps *(Vespa orientalis)*.

All sting challenges were conducted in the allergy unit with cardiac rhythm and blood pressure monitoring. An intravenous catheter was inserted into the cubital vein. Medication and

From The Allergy and Clinical Immunology Unit, Meir Hospital, Kfar Saba, and Tel-Aviv University Sackler School of Medicine.
Reprint requests: Arnon Goldberg, MD, Allergy and Clinical Immunology Unit, Meir Hospital, 44281 Kfar Saba, Israel.
J Allergy Clin Immunol 1997;100:139-41.
Copyright © 1997 by Mosby–Year Book, Inc.
0091-6749/97 $5.00 + 0 **1/54/82149**

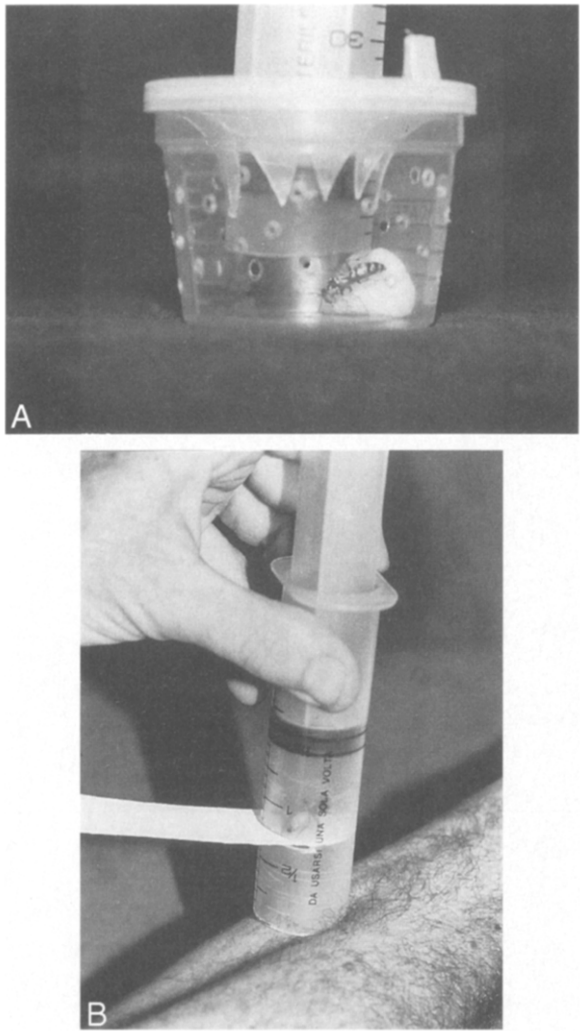


FIG. 1. Catching the insect **(A)** and challenging a patient **(B)** with the device.

medical and nursing staff were on hand. The insects were caught from an apiary or a nearby nest, and challenges were performed 1 to 5 hours after the insects had been collected. Insects were kept in a transparent plastic container perforated diffusely, together with cotton wool soaked with 5% sugar water. The container was sealed with a round, soft plastic cover, which was cut into 8 or 12 isosceles triangles.

A 50 ml disposable plastic syringe was perpendicularly cut, leaving out its pointed tip. Three centimeters above the edge of the syringe, a 1 mm wide slot was cut through the syringe wall. The round shaped edge of a cardboard ruler could then be inserted into the slot.

When the open lower edge of the syringe was inserted into the container, none of the insects could escape because of the elasticity of the cut cover (Fig. 1, *A*). When a single insect explored the inner part of the syringe, the ruler was inserted into the slot, leaving the insect isolated in the upper cell. The syringe was then removed from the container and applied to the volar aspect of the patient's arm. The ruler was then removed, and the syringe plunger was gently pushed, pressing the insect against the patient's skin (Fig. 1, *B*). When a sting was observed and sensed by the patient, the syringe was left unattached for 60 seconds, after which the insect was removed by applying thumb forceps around its head. In the case of honeybees, the stinger was removed from the skin together with the insect.

RESULTS

In all patients a local wheal and flare developed at the site of the sting. In two patients a large local reaction developed subsequently. Two patients had mild diffuse urticaria, which required no treatment. One of them was receiving maintenance immunotherapy at 3-month intervals, and in the other patient, 3-year immunotherapy had been discontinued 2 years earlier. A single patient in whom sting challenge was performed for diagnostic purposes experienced a moderate respiratory and cutaneous systemic reaction, which required administration of subcutaneous epinephrine and inhalation of terbutaline. All three systemic reactions were caused by honeybee stings.

All deliberate sting challenges were carried out uneventfully as previously described. None of the insects fled from the container or from the syringe. Three honeybees consistently "refused" to sting and were replaced by other bees.

DISCUSSION

Interest in performing deliberate insect sting challenge as a diagnostic procedure has recently increased. An increased use of this procedure is thus expected to take place among allergists treating patients allergic to venom. Many variables may affect the outcome of sting challenge. Differences regarding the insect include the actual volume of venom injected and the actual venom allergen content, which may vary from insect to insect and from sting to sting. The method of catching the insects and possible discharge of venom within the container or the syringe may also affect the outcome when our device is used. There is also a potential for differences in procedure by the operator of our device, such as the degree of pressure and length of contact between the insect and the skin. Another major pitfall may be an incorrect identification of the insect, if species are not collected by trained individuals. Performing this challenge without previous experience and using different techniques may be bothersome and occasionally dangerous because of unintended stings of the patient or an allergic bystander by a free flying insect. Trying to hold the insect by its legs may be technically difficult and may eventually result in the insect's escape. Holding the insect with thumb forceps may also result in varying degrees of pressure applied on the stinging organ, which may eventually result in a variable amount of venom delivered to the skin.

Although our device does not eliminate all of the above-mentioned variables, it does have some valuable advantages. First, it is very simple and can be "produced" by any allergist. Second, it is easy to operate and does not require any previous experience. Although not measured by us, the amount of venom delivered with each sting may be standard, as much as possible, because

of the equally distributed pressure applied on the insect's body by our device. When challenged, most of our patients were protected against repeated systemic reactions. Therefore we did not expect a high rate of systemic reactions. Nevertheless, two patients had diffuse urticaria, and one patient had a moderate systemic reaction. Taken together, the local wheal-and-flare reactions induced in all patients, the large local reactions, and the systemic reactions support the reliability of the device in inducing a sting and in delivering the venom into the patient's skin. Our device was also found to be safe because we did not observe any accidental, unintentional stings.

In conclusion, we think that our device proved to be safe and effective in performing sting challenges. It is also simple and easy to use, and if adopted and operated by all allergists performing deliberate challenges, it may contribute to the standardization of this procedure.

REFERENCES

1. Goldberg A, Confino-Cohen R, Mekori YA. Deliberate sting challenge as a diagnostic tool in highly selected venom-allergic patients. Ann Allergy Asthma Immunol 1995;75:30-2.
2. Blaauw PJ, Smithuis OLMJ, Elbers ARW. The value of an in-hospital insect sting challenge as a criterion for application or omission of venom immunotherapy. J Allergy Clin Immunol 1996;98:39-47.
3. Lichtenstein LM. A reappraisal of sting challenges: To whom should we offer venom immunotherapy? J Allergy Clin Immunol 1994;94: 137-8.