

Delayed hypersensitivity and allergic rhinitis

A negative study

**George W. Hutchinson, Major, MC, USA, and
Robert W. Griffiths, Major, MC, USA**
El Paso, Texas

In skin tests with pollen extract, antihistamine, and pollen-antihistamine combination in 20 adult patients with histories of typical hay fever upon exposure to Bermuda grass and large immediate skin test reactions to this pollen extract, altering or inhibiting the immediate wheal and flare reaction did not demonstrate a hidden tuberculin-like skin reaction.

Brostoff and Roitt¹ reported that delayed hypersensitivity developed to grass antigen in 4 of 6 patients with allergic rhinitis induced by grass pollens. They demonstrated tuberculin-like skin tests in their patients after blocking the immediate wheal and flare reaction by combining antihistamine (chlorpheniramine, 10 mg. per milliliter) with the skin test material. They postulated that the immediate reaction caused dilution of the antigen; by preventing this dilution, the delayed reaction was then demonstrable. In addition, they demonstrated the induction of lymphocyte transformation and the production of migration inhibition factor (MIF) when these patients' cells were exposed to grass pollen antigens.

However, in a group of allergic children, Go and associates² were unable to demonstrate delayed hypersensitivity skin reactions to grass pollens with the use of similar methods.

This study was undertaken to see if, with the use of Bermuda grass pollen and adult patients, Brostoff and Roitt's initial observation could be repeated.

MATERIALS AND METHODS

The 20 adult patients studied all had histories of typical hay fever on Bermuda grass exposure and large (greater than 8 mm. wheal) immediate skin test reactions to this pollen extract (100 protein nitrogen units [PNU] per milliliter). None had received hyposensitization and none had antihistamines for 24 hours prior to testing. The pollen antigen was aqueous Bermuda grass extract (Greer Laboratories, Lenoir, N. C.). All tests were intradermal, with a volume of approximately 0.02 ml. The control tests were done on one forearm with 10 PNU per milliliter concentration of the pollen extract, chlorpheniramine 25 mg. per milliliter, and the buffered saline used to dilute the extract. Three combined pollen-antihistamine solutions

From the Department of Medicine, Allergy/Immunology Service, William Beaumont General Hospital.

Received for publication Oct. 5, 1974.

Reprint requests to: Major Hutchinson, William Beaumont General Hospital, El Paso, Texas 79920.

TABLE I. Results of intradermal skin tests with Bermuda extract, antihistamine, and combined Bermuda extract and antihistamine

Time skin tests were read	Pollen alone 10 PNU/ml.	Chlorpheniramine 25 mg./ml.	Pollen + chlorpheniramine 25 mg./ml.		
			10 PNU/ ml.	100 PNU/ ml.	1,000 PNU/ ml.
20 min.					
Wheal (mm.)	9.9	5.3	6.5	8.3	11.3
Flare (mm.)	30.0	6.4	10.0	16.1	25.0
24 hr.	0	0	0	0	Soft edema in 6 (7 cm. average)
48 hr.	0	0	0	0	0

Values are averages for 20 patients tested. Individual reactions were measured in two diameters and averaged. The pollen-antihistamine combination blocked 80 per cent of the 10 PNU, 50 per cent of the 100 PNU, and 20 per cent of the 1,000 PNU reactions. All buffered saline controls were negative. See text for details of the edematous reactions at 24 hours.

were applied to the other forearm. These consisted of 10, 100, and 1,000 PNU per milliliter pollen extracts each of which contained chlorpheniramine, 25 mg. per milliliter. The concentration of chlorpheniramine was decided by trial and error in other patients. The concentration of chlorpheniramine used by the other investigators (10 mg. per milliliter) did not adequately block the immediate wheal and flare reaction in our study. We used three concentrations of the pollen extract in an attempt to ensure adequate antigenic challenge and to see if there might be a dose relationship in the production of delayed reactions to the grass pollen. All skin tests were read at 20 minutes, 24 hours, and 48 hours.

RESULTS

The results of these tests are shown in Table I. None of the patients had demonstrable skin reactions at 48 hours. The first 4 patients tested, when next seen at 24 hours, had developed reactions consisting of heat, extensive erythema, and an average of 7 cm. of soft, subcutaneous edema which centered around the 1,000 PNU per milliliter pollen-antihistamine test site. These patients had noted gradual progression from the immediate skin reaction to the reaction described above. Historically, this was maximal at approximately 12 hours and subsided by 36 hours. None showed residual of this reaction at 48 hours. In an attempt to suppress this reaction, the remaining 16 patients were started on oral chlorpheniramine, 4 or 8 mg. every 6 hours, immediately after the 20 minute skin test reading. They were instructed to continue the oral antihistamine for 48 hours. Only 2 patients of this group developed test site edema at 24 hours.

It was interesting that in all but one patient chlorpheniramine alone produced a wheal and flare reaction. These reactions ranged in size from 3 to 12 mm. wheals and 0 to 25 mm. flare. Chlorpheniramine mixed with the antigen significantly altered the immediate reaction in all patients when compared to the positive control. A reaction was considered blocked if the immediate wheal and flare produced by the antigen and antihistamine was no larger than that produced by the antihistamine alone. In sixteen patients (80 per cent) the 10 PNU reaction was completely blocked. In 10 patients (50 per cent) there was blocking of the 100 PNU reaction, and in 4 patients (20 per cent) there was blocking of the 1,000 PNU reaction.

Our results are in agreement with those of Go and associates, the only major difference between our studies being that we tested adult patients as did Brostoff and Roitt. Altering or inhibiting the immediate wheal and flare reaction did not demonstrate a "hidden" tuberculin-like skin reaction.

REFERENCES

- 1 Brostoff, J., and Roitt, I.: Cell mediated (delayed) hypersensitivity in patients with summer hay fever, *Lancet* 2: 1269, 1969.
- 2 Go, S., Michaels, D., and Ellis, E.: Delayed hypersensitivity to pollen, *Lancet* 1: 1115, 1970.