

Relationship between nasal and conjunctival tests in patients with allergic rhinitis

C. H. O. MALMBERG, E. E. A. HOLOPAINEN *and*
B. S. M. STENIUS-AARNIALA

*Departments of Otolaryngology and Pulmonary Diseases,
Helsinki University Central Hospital, Helsinki, Finland*

(Received 6 February 1978; accepted for publication 21 February 1978)

Summary

Simultaneous conjunctival and nasal provocation tests, a total of 174 test pairs, were carried out in fifty patients with allergic rhinitis, using serially diluted antigen solutions of birch, Timothy grass and mugwort pollen, as well as cat and dog dander. The nasal mucosa was found to be more sensitive than the conjunctival mucosa in ninety-six test pairs (55%). This differs from earlier reports. Nasal reaction only was observed in twenty-nine instances (17%). Posterior rhinomanometry was also used to evaluate test reactions, but was found to yield little additional information. In 43% of nasal provocation tests, which according to other criteria were positive, the rhinomanometric results were negative.

Despite a fairly good correlation between the results obtained by nasal and conjunctival challenge, the results point to organ specificity in type I reactions. Provocation tests, if indicated in a thorough allergy evaluation, should be performed in the shock organ.

The provocation methods and interpretation of reactions of this study differ from those of earlier reports. Comparison of results is difficult and standardization of methods is needed.

Introduction

Provocative testing is (often) regarded as the most relevant diagnostic method in allergy (Juhlin-Dannfelt, 1950; Halpern, Holman & Whittaker, 1961; Connell, 1967, 1968; Naumann, Naumann & Schubert, 1969; Holopainen, Tarkiainen & Malmberg, 1976). On account of the technical difficulties and the time required for performing nasal provocations, the complications which may ensue and the difficulties in interpreting the results, attempts have been made to substitute the much easier conjunctival provocation test for the nasal test (Fineman, 1926; Tuft *et al.*, 1959). Comparative

Correspondence: Dr Henrik Malmberg, Department of Otolaryngology, Meilahti Hospital, 00290 Helsinki 29, Finland.

studies on provocation tests have, indeed, demonstrated a good correlation between these two methods, the conjunctiva usually being the more sensitive organ (Feinberg, Stier & Grater, 1952; Ingestad, 1971). In nasal challenge, rhinomanometric measurements of nasal resistance changes are widely used for the purpose of obtaining additional information in the interpretation of test results (Aschan & Drettner, 1958; Naumann *et al.*, 1969; Taylor & Shivalkar, 1971; Münzel & Behbehani, 1976).

In the present study nasal and conjunctival provocation tests were carried out in rhinitis patients, the aim being, firstly, to compare nasal and conjunctival reactions provoked by the same serial dilutions of antigens and, secondly, to correlate the results obtained in these two target organs with data from the history and with the skin test and RAST results.

Materials and methods

Materials

Fifty patients, aged 10–68 years, the mean age being 32 years, were tested by nasal and conjunctival provocation. All the patients had nasal symptoms, which in twenty-eight of them were combined with conjunctival and in thirty with asthmatic symptoms. The patients were all atopics (Pepys, 1975) and they were selected for the present study on the basis of previous skin testing, because they could be expected to react to at least one of the allergens to be investigated. None of the patients had been hyposensitized with any of these allergens. Provocative testing was performed at a time when the patients were practically free from symptoms.

The allergens tested were birch, Timothy and mugwort pollen, described by Stenius-Aarniala *et al.* (1978b), and dog and cat dander, provided by Dome Laboratories, Slough, England. The Dome extracts for prick-testing and the animal dander extracts for the provocation tests contained 50% glycerol. All other solutions used for the *in vivo* tests were glycerol-free. The serial dilutions from the stock solution were 1/10, 1/100, 1/1000 and 1/10,000.

Methods

Methods and evaluation criteria used in the skin testing (by the prick technique) and in the RAST are described elsewhere by Stenius-Aarniala *et al.* (1978b). Nasal provocation was performed by the local application method (Holopainen & Siirala, 1974), where 0.1–0.2 ml of antigen solution is absorbed into a small bud of cotton, which is applied to the mucosal membrane of the inferior turbinate. If no reaction was observed within 15 min, higher concentrations of the serial dilutions were applied successively, until the stock solution was reached or a reaction occurred. In the instance of a positive reaction, provocation was discontinued for 48 hr. The result was considered positive (+) when at least two of the following criteria were satisfied: sneezing, itching, discharge, subjectively noted obstruction of the nose or a rhinoscopic finding of changes in the nasal mucosa (swelling or colour change). When only one of these criteria was satisfied, the result was regarded as doubtful ($\pm$). Posterior rhinomanometry, consisting of simultaneous recording of pressure difference and air flow through the nose, was performed with Siemens Elema apparatus, as described by Masing (1967). Nasal flow was measured at a differential pressure of 10 mmH₂O. A diminution in nasal flow of 25% or more indicated a positive provocation result, even when the result was negative according to other criteria of positivity used in this study.

Conjunctival provocation was done in the eye opposite to the challenged nostril simultaneously with the nasal provocation. The concentration of the antigen solution was always ten times lower than the dilution tested in the nose. One to two drops of antigen solution was instilled into the inferior recess of the lids. Criteria of positivity were itching, injection of the conjunctiva and lacrimation. A positive result (+) was defined when two of these were observed and the result was doubtful ($\pm$) when only one symptom was noted.

The diluent served as a control solution and was first applied to both sites of provocation. Marked uncomfortable reactions in both target organs were treated locally with a 1/1000 adrenalin solution.

Several allergens or different preparations of the same allergens were tested on most of the patients. Thus 174 pairs of nasal and conjunctival provocation tests were available for analysis.

Results

The reactivity of the nasal mucosa is compared with that of the conjunctiva in Fig. 1 and Table 1. Only in fifteen pairs of simultaneous provocation tests (9%) did conjunctival provocation elicit a positive reaction with an allergen solution weaker than the one provoking a nasal reaction. In the majority of instances of provocation (54%), the nasal mucosa was the more sensitive target organ. The difference is statistically significant. Conjunctival provocation yielded negative results in contrast to a positive nasal reaction in twenty-nine pairs of provocation tests (17%) performed on eighteen patients. Nine of these patients had a negative history of conjunctivitis. History and provocation gave concordant results in 63% of the nasal and in 56% of the

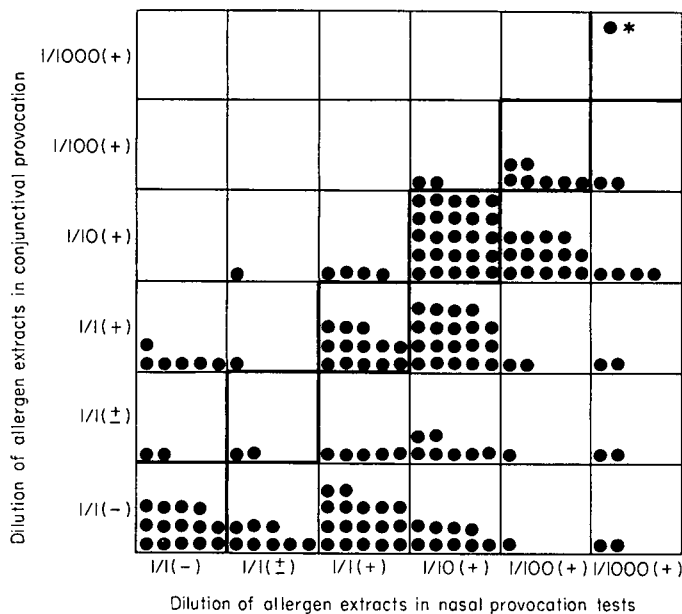


Fig. 1. Comparison between nasal and conjunctival tests (174 pairs of provocations). Test results: (-) negative; ($\pm$) doubtful; and (+) positive. * Dilution of allergen in conjunctival provocation 1/10,000.

Table 1. Comparison between nasal and conjunctival provocation tests. Variation in reactions to different allergens: birch, Timothy grass, mugwort and animal dander

Allergen	Number	Concordant results (%)	Nasal test more sensitive than conjunctival test (%)	Conjunctival test more sensitive than nasal test (%)	P*
Birch	40	30	63	7	<0.01
Timothy	55	38	56	6	<0.01
Mugwort	68	35	49	16	<0.01
Animal dander	11	45	55		<0.05
Total	174	36	54	10	<0.01

* Binomial distribution.

Table 2. Analysis of cases with negative nasal or conjunctival provocation results and positive corresponding skin test results. Correlations with provocation in the other target organ and with the RAST results

Nasal provocations (n = 10)			RAST result	Conjunctival provocations (n = 21)		
Conjunctival test (+) (±) (−)				Nasal test (+) (±) (−)		
2	—	4	Positive	8	3	5
2	—	2	Negative	3	—	2

conjunctival provocation tests. Although the skin tests were positive, negative results were obtained by provocation in sixteen nasal (11%) and in thirty-six conjunctival (25%) tests. These negative provocation results were compared with the provocation results in the other target organ and with the RAST. Those cases in which the skin and provocation tests were performed with allergens diluted from the same batch of allergens are presented in Table 2. Conversely, nine positive nasal and three positive conjunctival provocation results were noted in instances where the corresponding skin test was negative or doubtful.

Rhinomanometry was used in connection with 128 provocation tests. In 54% of cases the results were concordant but in 43% rhinomanometry yielded negative results in tests which according to other criteria were positive. Conversely, rhinomanometric results were positive in two tests which by other criteria were negative, and in two where the result was doubtful (3%).

No side effects attributable to the provocation were noted.

Discussion

On challenge, the nasal mucosa gave a positive result more frequently than the conjunctival mucosa and the concentration of the allergen solution necessary to provoke a reaction was usually lower. All patients of the present series had a positive history of nasal allergy, but only twenty-eight out of fifty had eye symptoms. However,

even in the group with symptoms in both target organs, this greater sensitivity of the nasal mucosa was apparent. This observation differs from earlier results obtained by Feinberg *et al.* (1952) and Ingestad (1971). The method of provocation and the slightly different criteria of positivity used in the present study may explain the differences in the results obtained. The local application of antigen solution by means of a small cotton bud may produce a greater concentration of antigen on a small area and a more prolonged provocative effect in comparison with other methods of application. On the other hand, it is possible to inspect the local effect carefully by rhinoscopy, and even a small amount of secretion and local changes in the nasal mucosa, such as swelling and change in colour, can be noticed. In addition, the use of higher concentrations of antigen solution, which could cause very marked reactions or side effects, can be avoided.

The use of rhinomanometry for the purpose of evaluating provocation reactions did not yield much additional information on nasal reactivity. Negative results were recorded in 43 % of the tests which were positive according to other criteria. This again may depend on our method of restricted local antigen application, and alert observation of other signs of response (such as local swelling of the mucosa, discharge and itching) means that they are observed before such a concentration of antigen is reached as would affect the total nasal resistance. Posterior rhinomanometry, where the total resistance is measured, may not be as sensitive a method as the anterior one, by which only one nostril is tested but, on the other hand, false positive results (due, for instance, to nasal cycle or distortion of the alae) are eliminated (Naumann *et al.*, 1969; Münzel, 1976; Holopainen *et al.*, 1976). The requirement of a fall in nasal flow of 25 % or more, which was used as a criterion of positivity, may be unnecessarily strict. Finally, it may be pointed out that the allergens tested were pollens and animal danders, which, in our experience, tend to produce symptoms of running and itching, while obstruction of the nose is the predominant symptom in house dust allergy.

Positive provocation reactions were found in patients with negative skin reactions and negative RAST results. On the other hand, provocation yielded negative results in patients with positive skin tests and/or RAST. Both these results may depend on target organ specificity (Fineman, 1925; Feinberg *et al.*, 1959; Ingestad 1971; Stenius-Aarniala *et al.*, 1978a), and when provocation is indicated in careful allergy examination it should, therefore, be carried out in the appropriate shock organ.

References

- ASCHAN, G. & DRETTNER, B. (1958) Nasal obstruction at provocation experiments in patients with hay fever. *Acta oto-laryngologica*, Suppl. 140, 91.
- CONNELL, J.T. (1967) Quantitative intranasal pollen challenges. *Journal of Allergy*, **39**, 358.
- CONNELL, J.T. (1968) Quantitative intranasal pollen challenge. *Journal of Allergy*, **41**, 123.
- FEINBERG, S.M., STIER, R.A. & GRATER, W.C. (1952) A suggested quantitative evaluation of the degree of sensitivity of patients with ragweed pollinosis. *Journal of Allergy*, **23**, 387.
- FINEMAN, A.H. (1926) Studies in hypersensitiveness. XXIII. A comparative study of the intradermal, scratch, and conjunctival tests in determining the degree of pollen sensitivity. *Journal of Immunology*, **11**, 465.
- HALPERN, S.R., HOLMAN, J. & WHITTAKER, C. (1961) The correlation between skin and respiratory mucous membrane tests with moulds in allergic rhinitis. *Annals of Allergy*, **19**, 1407.
- HOLOPAINEN, E. & SIIRALA, U. (1974) Das Nasenlaboratorium, Untersuchung von verschiedenen Rhinitisformen. *Monatsschrift für Ohrenheilkunde und Laryngo-Rhinologie*, **108**, 361.
- HOLOPAINEN, E., TARKIAINEN, E. & MALMBERG, H. (1976) Nasal challenge. *Rhinology*, **14**, 181.
- INGESTAD, R. (1971) Konjunktivaltestets värde vid utredning av allergisk rinit och astma. *Läkartidningen*, **68**, 3220.

- JUHLIN-DANNFELT, C. (1950) On the significance of exposure and provocation tests in allergic diagnostics. *Acta medica scandinavica*, **138**, Suppl. 239, 320.
- MASING, H. (1967) Die Rhinomanometrie. *Electromedica*, **2**, 6.
- MÜNZEL, M. & BEHBEHANI, A. (1976) The diagnostic value of intranasal tests in allergic rhinopathy. *Rhinology*, **14**, 37.
- NAUMANN, H.H., NAUMANN, W.H. & SCHUBERT, B. (1969) Zur Methodik des Schleimhauttestes bei Nasenallergie. *Zeitschrift für Laryngologie, Rhinologie, Otologie und ihre Grenzgebiete*, **48**, 198.
- PEPYS, J. (1975) Atopy. *Clinical Aspects of Immunology* (eds P. G. H. Gell, R. R. A. Coombs and P. J. Lachmann), 3rd edn, p. 877. Blackwell Scientific Publications, Oxford.
- STENIUS-AARNIALA, B.S.M., MALMBERG, C.H.O. & HOLOPAINEN, E.E.A. (1978a) Relationship between the results of bronchial, nasal and conjunctival provocation tests in patients with asthma. *Clinical Allergy*, **8**, 403.
- STENIUS-AARNIALA, B.S.M., MALMBERG, C.H.O., HOLOPAINEN, E.E.A. & BJÖRKSTEN, F. (1978b) *In vivo* tests with pollen extracts previously investigated by means of direct RAST titration allergen assay. *Clinical Allergy*, **8**, 411.
- TAYLOR, G. & SHIVALKAR, P.R. (1971) Changes in nasal airways resistance on antigenic challenge in allergic rhinitis. *Clinical Allergy*, **1**, 63.
- TUFT, L., ETTELSON, L.N., GUPTA, K. & KRUEGER, C. (1959) Eye tests with inhalant allergens. *Journal of Allergy*, **30**, 492.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.