

# Specific nasal provocation test with powder allergen

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**F. A. Salzano**

ENT Department, University "Federico II",  
Naples, Italy

Reported here are the results of a large-scale trial conducted under the guidance of Prof. Giovanni Motta, which I coordinated. A total of 656 patients with nasal hyperreactivity were recruited in 51 Italian centres (18 in the north of Italy, 20 in central Italy and 13 in the south). The trial's results were as follows. 1) A clear clinical prevalence of sensitization to different allergens in the different areas of Italy, which could be roughly classified thus: a) in Northern Italy birch and grasses were the main species; b) in Central Italy mites prevailed but oleaceae were also significant; c) in Southern Italy parietaria and oleaceae were the prevailing species. 2) Most cases were sensitive to several allergens, although a considerable proportion (22%) actually presented reactions only to one, the main allergen. 3) Taking account of the patients sensitive to only one allergen and those responding to a main allergen, the proportion of patients reacting clinically to only one allergen rises to 64%. 4) The specific nasal provocation test (sNPT) offers specificity comparable to *in vivo* diagnostic methods such as the prick test, and *in vitro* methods such as RAST, but is much more sensitive. 5) The sNPT can be done in any season. 6) The sNPT is highly specific below a threshold value of nasal reactivity, which can be identified for each allergen studied and expressed in Allergenic Units. 7) In patients in whom the prick test shows multiple sensitivity, the specific NPT identifies the allergen presumably responsible for the nasal reactions (main allergen). In the light of these findings double-blind specific immunotherapy was started, to last 1 year, in 107 patients (49 given placebo and 58 active treatment), with nasal allergy to grasses, parietaria and mites. The results of this treatment were as follows: 74.1% of patients presented a reduction in nasal resistance, measured by dynamic anterior rhinomanometry, indicating relief of nasal obstruction; mucociliary transport time became normal in 81% of patients, meaning that rhinorrhoea had become less marked; there was a significant rise in the nasal reactivity threshold in 74.1% of patients, illustrating the degree of desensitization achieved; nasal IgA increased in 62.5% of patients and IgG in 55.2% indicating improvement in the local immunological picture. No such improvements were detectable in the patients given placebo. In conclusion, therefore, the findings of this trial in allergic rhinitis underline that the specific NPT proved more sensitive than other *in vivo* and *in vitro* diagnostic methods and is unquestionably a fundamental investigational approach for assessing nasal allergies, identifying the allergens causing the symptoms and setting up rational local immunotherapy. The sNPT also showed the efficacy of specific intranasal immunotherapy.

Key words: nasal provocation test;  
allergic rhinitis; nasal immunotherapy.

F.A. Salzano  
Clinica ORL  
Via S. Pansini 5  
80131 Napoli  
Italy  
Tel: 39 81 7463227 - 7463489  
Fax: 39 81 5467447

The causal treatment of allergic rhinitis needs a correct and careful diagnostic approach based on the study of morphological changes by means of an anterior active dynamic rhinomanometric test (9, 11, 12, 15, 16), on the identification of the infective agents (bacteria, micetes, chlamydiae, etc.) (11, 15,

16) and on the determination of specific causal agents that must be done by means of a specific nasal provocation test (sNPT) (4, 9, 10, 14).

After identification of the sensitization threshold of responsible allergens by means of nasal provocation tests and determination, in polysensitive

patients, of the principle allergen provoking the clinical picture of allergic vasomotor rhinitis, we can plan a local immunotherapy for this particular allergen. This treatment consists of the nasal administration of progressively increasing dosages of allergen and following induction of a tolerance condition for the same allergen with the reduction or disappearance of the allergic symptomatology.

## Personal studies

Our findings on nasal immunotherapy are related to the following.

### *Vasomotor allergic rhinitis, pollens and mites*

I. A preliminary research carried out on 20 patients affected by vasomotor allergic rhinitis due to pollens (grass and pellitory) and to mites (6, 11); in all these subjects we excluded the presence of morphological changes or infective factors (bacteria, micetes and chlamydiae) and we used the nasal provocation test evaluated by means of rhinomanometry to establish the exact sensitization threshold, corresponding to the dosage of allergen which can provoke an increase of 100% of the nasal resistance values compared with those documented in basic conditions. The patients were treated over 1 year using allergens in solution administered by drops of increasing dosages in the nasal cavities. The results we obtained after 1 year of treatment were completely satisfactory in all the patients: we found a rise in the nasal allergic sensitization threshold of approximately 40 times compared to the values shown at the beginning of the treatment, with a great improvement of the clinical symptomatology.

This kind of local immunotherapy requires an immediate preparation of allergenic solution because of the drop in the allergenic power and a periodical sanitary intervention to establish the allergene dosage to be administered in the nasal cavity.

II. A group of investigations about the epidemiology and diagnosis of nasal allergy was performed by 51 centres, distributed all over Italy, and involved 656 patients.

In the study the following were found:

- 1) a clear prevalence of sensitization to different allergens in the different areas of Italy, which could be roughly classified as follows:
  - in Northern Italy grasses were the main species (Fig. 1a);
  - in Central Italy dust mites prevailed (Fig. 1b);
  - in South *parietaria* (Fig. 1c);

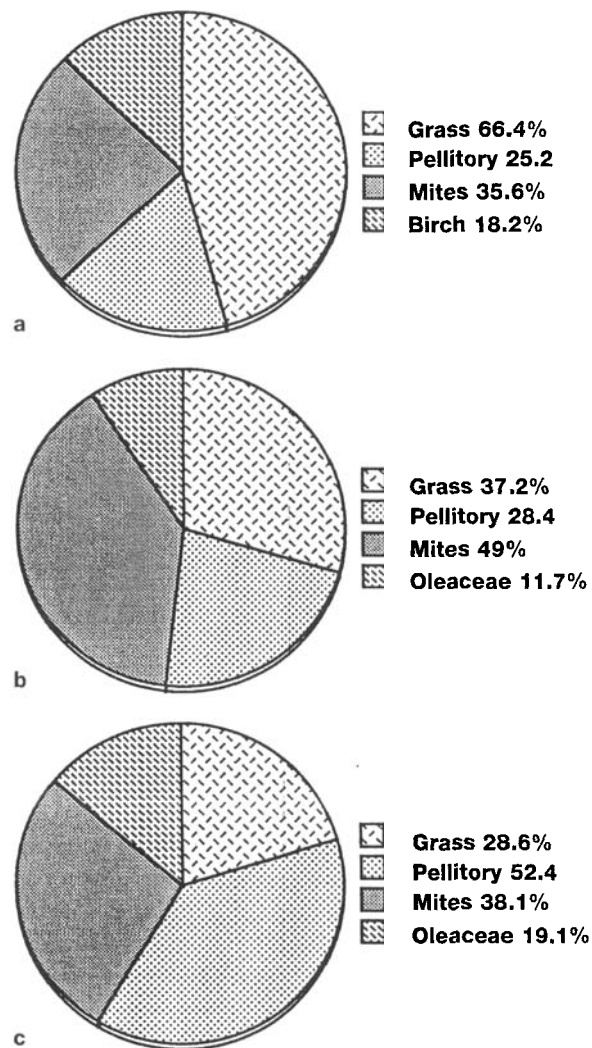


Fig. 1. Prevalence of sensitization to various inhalant allergens in northern, central and southern Italy. a) Northern Italy, 143 allergic patients examined. b) Central Italy, 102 allergic patients examined. c) Southern Italy, 63 allergic patients examined.

with a significant presence of:

- birch in the North;
  - oleaceae in the Centre and South of Italy.
- 2) Most cases were sensitive to several allergens, although a considerable proportion (22%) actually presented reactions only to one, the main allergen.
  - 3) Taking account of the patients sensitive to only one allergen and those responding to the main allergen, the proportion of the patients reacting clinically to only one allergen rises to 64%.
  - 4) The specific nasal provocation test (sNPT) offers specificity comparable to *in vivo* diagnostic methods such as a prick test, and *in vitro* methods such as RAST, but is much more sensitive.
  - 5) The sNPT can be done in any season.
  - 6) The sNPT is highly specific below a threshold

value of nasal reactivity, which can be identified for each allergen studied and expressed in allergenic units (AU). We have a threshold dose of about 40 AU in allergic patients and about 70 AU in non-allergic patients (clinically evaluated).

- 7) In patients in whom the prick test shows multiple sensitivity, the specific NPT identifies the allergen presumably responsible for the nasal reaction (the main allergen).

*III.* The results came from a multicentric study involving eight other centres; nasal immunotherapy with the allergen in powder form was carried out using a double-blind method over 1 year. The use of the allergen in powder form (Allerkin, prepared by Lofarma, an Italian company specializing in immunotherapy of allergic diseases) shows remarkable stability of the allergen, the concrete possibility of self treatment at home and less frequent medical checks.

In this research we followed 107 patients (49 placebo and 58 active) affected by nasal allergy due to grass, pellitory and mites. At the beginning of the treatment permanent obstruction and infective agents were not present in these subjects.

The allergen (in the active group) or the lactosio (in the placebo group) in powder form were administered according to the following plan:

*First phase of progressive increasing dosages* (2.5, 5, 10, 20, 40, 60, 80, 120, 160, 240). During this phase we carried out a nasal administration of the powder on alternate days and in alternate nostrils until the maximum dosage was reached; each dosage was administered six times.

*Second phase of maintenance with maximum possible dosage.* This was administered weekly in alternate nostrils. To evaluate the results of the treatment we considered the following parameters:

- nasal provocation test which shows the taking place of desensitization through the increase of the allergenic threshold dosage;
- nasal resistance for the obstruction, studied by rhinomanometry;
- MCT (mucociliary transport) for the rhinorrhoea; and
- determination of nasal IgG and IgA (blocking antibodies) such as index of local immunological changes.

The results were as follows:

- there was a significant rise in the nasal reactivity threshold in 74.1% of patients, illustrating the degree of desensitization achieved (Fig. 2);
- 74.1% of patients presented a reduction in nasal

resistances, measured by active anterior rhinomanometry, indicating relief of nasal obstruction (Fig. 3); and

- mucociliary transport time became normal in 81% of patients, meaning that rhinorrhoea had become less marked (Fig. 4).

No such improvements were detectable in the placebo patients. Finally, the immunological evaluation of nasal antibodies showed an increase (but not significant) in IgG and IgA which was more evident in the active group than in the placebo group.

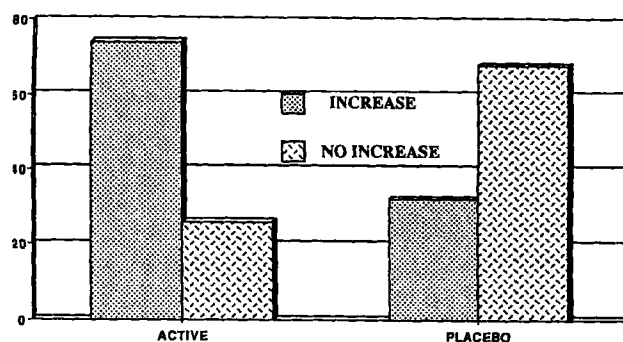


Fig. 2. Threshold dose in the active and in the placebo group: there was a significant rise ( $P < 0.001$ ) in the nasal reactivity threshold in the active group (index of desensitization).

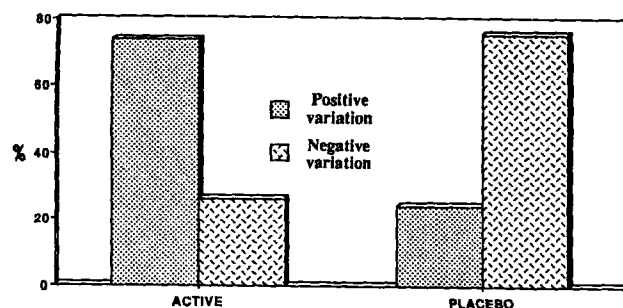


Fig. 3. Nasal resistance in the active and in the placebo group: there was a significant positive variation (reduction of nasal resistance,  $P < 0.001$ ) in the active group (index of nasal obstruction).

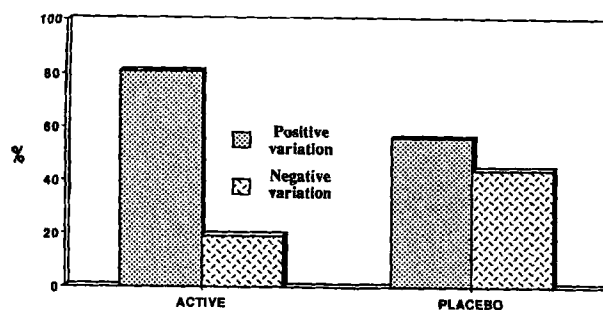


Fig. 4. Mucociliary transport in the active and in the placebo group: there was a significant positive variation (decrease of mucociliary transport time,  $P < 0.001$ ) in the active group.

## Conclusions

In conclusion, therefore, the findings of the above-reported studies in allergic rhinitis underline the following.

- 1) The need for a) a precise history and clinical assessment; and b) correct identification of allergens. The appropriate tests must be used to establish the relationship between clinical symptoms and causal allergens.

The specific NPT proved more sensitive than others *in vivo* and *in vitro* diagnostic methods and is unquestionably a fundamental investigational approach for assessing nasal allergies, identifying the allergens causing the symptoms and setting up rational local immunotherapy.

The sNPT also showed the efficacy of specific intranasal immunotherapy. A new, simplified sNPT, based on the nasal challenge with one or two single allergen dosages, is now under clinical trial.

- 2) The effectiveness of local immunotherapy (1, 2, 5, 7, 8, 13, 17). This kind of treatment causes an increase of threshold dosage and a significant decrease of hyperreactivity symptoms (rhinorrhoea and obstruction). On the basis of these results there are, of course, immunological reactions also expressed by the increase of nasal IgG and IgA.

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