

Local nasal desensitization in allergic rhinitis

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Summary

Persistent reduction in nasal sensitivity was induced in most subjects suffering from allergic rhinitis by repeated nasal allergen challenge. Patients so treated failed to respond by increases in nasal airways resistance, sneezing or nasal discharge when challenged with doses of allergen which previously provoked such responses. Disodium cromoglycate did not facilitate the induction of local desensitization although it blocked the unpleasant symptoms of nasal challenge. Diminished sensitivity persisted at least for several months and test groups had significantly lower symptom scores during the pollen season when compared with control subjects. It is suggested that a local secretory IgA response may be involved in the reduction in sensitivity.

Introduction

During studies on the nasal response to allergen challenge we observed that a proportion of subjects became progressively less responsive after several nasal challenges (Taylor & Shivalkar, 1971a). Analysis of the relationship between nasal airway resistance and allergen dose in 108 subjects revealed that twelve subjects responded in this manner. Four of these twelve subjects were rechallenged 1 year later and still remained unresponsive. Further, though initially pollen-sensitive and suffering from typical hay fever, they had remained virtually free of symptoms during the summer months of the intervening year. During the years 1969 and 1970 we carried out laboratory studies on the protective effect of disodium cromoglycate (DSCG) in allergic rhinitis (Taylor & Shivalkar, 1971b) and were able to compare the incidence of local nasal 'desensitization' following repeated nasal challenge in these years. The year 1970 produced a much higher proportion of desensitized subjects. The major differences in procedure between the two years were the greater average number of allergen challenges and the much greater use of nasal DSCG in 1970. We report here attempts to increase the incidence of local nasal desensitization, to study its clinical value during a pollen season and to investigate the role of nasal DSCG on the induction of local nasal desensitization.

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Methods

Subjects

University students who believed that they were suffering from seasonal allergic rhinitis were asked to volunteer for the investigation. The diagnosis was confirmed by history, examination, skin testing (using the modified prick technique), and by nasal challenge. A total number of forty-nine subjects were investigated, but not all completed the full schedule. The mean age was 19.5 years with a range of 18–27, and the mean length of history of allergic rhinitis was 11.6 years (range 3–17 years).

Laboratory protocol

In order to avoid environmental challenge with grass pollen the investigations were carried out during the winter months. The NAR_{200} dose of mixed grass pollen extract was first determined in all subjects using the method of Taylor & Shivalkar (1971a). The subjects were then divided randomly into three groups.

Group 1 received at each attendance 20 mg lactose powder to each nostril followed by the appropriate NAR_{200} dose of grass pollen extract.

Group 2 received 10 mg lactose powder plus 10 mg disodium cromoglycate (DSCG) to each nostril followed by the NAR_{200} dose of grass pollen.

Group 3 received the same powder as Group 2 (lactose + DSCG) followed by nasal sprays of isotonic saline.

The procedure was repeated four to eight times with intervals of 2 or 3 days between applications. On each attendance changes in nasal airways resistance were observed over a 15 min period after challenge. In addition a symptom score was recorded. This was determined according to the subject's response to nasal challenge. Sneezing was evaluated by counting the number of sneezes: no sneezing—score 0; up to five sneezes—score 1; six to ten sneezes—score 2; more than ten sneezes—score 3. Nasal discharge was scored arbitrarily as nil, slight, moderate and severe, scoring 0, 1, 2 and 3 respectively. The number of paper handkerchiefs required after challenge gave a good indication of the degree of nasal discharge. Nasal obstruction was evaluated symptomatically as nil, some unilateral obstruction, or complete obstruction giving scores of 0, 1 and 2 respectively. The total symptom score could therefore vary from 0 to 8.

After completing this schedule the subjects were challenged within 4 days with the previously determined NAR_{200} dose of grass pollen extract and the NAR response and symptoms score determined. The subjects were again re-challenged after an interval of several weeks (mean interval 48 days). As this period was during the months of December and January it is very unlikely that any further exposure to pollen had occurred. Re-challenge with similar recording of NAR changes and symptom score was with the NAR_{200} dose, with twice this dose, and in some subjects with four times this dose. In addition, the specificity of any local desensitization induced to grass pollen was investigated by challenging subjects with mixed 'shrub' pollens (Bencard B1) extract and with mixed tree pollen extract (B3). So that there should be no question of local desensitization to these allergens induced during previous determination of nasal sensitivity this was not carried out. We therefore used an arbitrary concentration of both (1/5). Although the subjects all gave positive weal and flare skin responses to B1 and B3 extracts it was appreciated that nasal sensitivity would not necessarily correlate with these positive skin tests.

Protocol of clinical trial

The effects of the three schedules were evaluated clinically during the pollen season of 1971. Subjects were provided with tablets of 4 mg chlorpheniramine maleate and diary cards. They were instructed to fill in the cards commencing on 24 May 1971 and continuing for a 6 week period. They were allowed to take one to three tablets of chlorpheniramine daily as necessary, but were asked to limit the usage of this drug as much as possible. The diary cards recorded the following information.

Name

Sneezing, nasal discharge, nasal obstruction, eye irritation and watering were graded daily by the subject on the following scheme:

- 0 complete absence of symptoms
- 1 mild symptoms which do not interfere with normal activities
- 2 moderate symptoms which interfere to some extent with normal activities
- 3 severe symptoms which prevent normal activities

For each day: number of antihistamine tablets taken, and answers to the following questions:

- Was throat irritation present today?
- Did you have any breathlessness today?
- Did you have any wheezing today?
- Did you have any cough today?

Each parameter recorded on the diary cards was assessed separately. The score of each group were compared using the Mann Whitney U test.

Results*Laboratory studies*

Local desensitization was considered to have been achieved if the NAR failed to rise above the baseline level during a 15 min period after challenge with the NAR₂₀₀ dose of allergen previously determined for the subject. Using this rather strict criterion local desensitization was found in a high proportion of both groups 1 and 2 but not group 3. The results of challenge immediately after the schedules described is presented in Table 1.

Using the Fourfold Table Test to compare the incidence of desensitization in the three groups no significant difference was shown between groups 1 and 2 ($P > 0.2$) thus suggesting that DSCG does not facilitate local desensitization to any significant degree. Both groups 1 and 2 differ highly significantly from group 3 ($P \leq 0.002$ in both cases). The one subject in group 3 who was desensitized had a relatively insensitive nasal mucosa on initial testing (NAR₂₀₀ dose 1/2.5) and required a total of six increasing challenges before a significant rise in NAR occurred. It is likely that this unusually large number of challenges with allergen before the schedule commenced could account for his desensitization. The evidence strongly suggests that administration of allergen is necessary for the induction of local desensitization.

In group 1 it was possible to determine after what number of doses of allergen the expected NAR response failed to occur. Fig. 1 shows successive responses to nasal challenge in group 1 subjects. The allergen-induced NAR response in the majority of group 2 subjects (77%) was blocked by the previous administration of DSCG. Hence

only when the schedule was complete and an unprotected challenge was given could the nasal sensitivity be determined in group 2 subjects.

Table 2 compares the nasal sensitivity state after four administrations of allergen with that after eight. All group 1 subjects are included but only those in group 2 who

Table 1. To show the proportion of subjects locally desensitized in the three groups when challenged with the NAR_{200} dose of allergen

Group	Desensitized	Not desensitized	Total
1 Lactose + allergen	12	3	15
2 DSCG + allergen	14	3	17
3 DSCG + saline	1	9	10

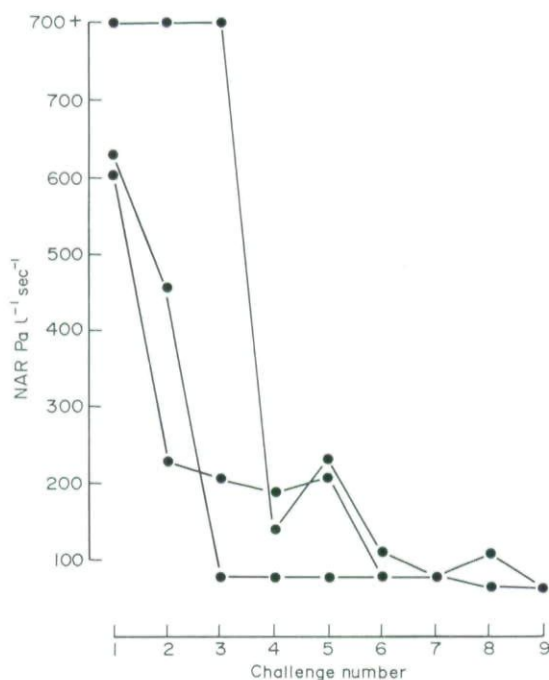


Fig. 1. Estimation of peak nasal airways resistance during the 15 min period following serial challenges at intervals of 2–3 days with the NAR_{200} dose of grass pollen allergen in three subjects of group 1.

Table 2. To show the proportion of subjects in groups 1 and 2 who had lost nasal sensitivity after four and after eight doses of allergen

	Not desensitized	Desensitized
After four doses	9	11
After eight doses	1	15

were challenged without DSCG after four or after eight doses of allergen. A significant increase in the incidence of local desensitization is found with the larger number of doses ($0.05 > P > 0.02$).

Repeat challenges with grass pollen extract were carried out approximately 6 weeks after completing the initial schedule. Nasal challenge with the NAR_{200} dose in seventeen desensitized subjects showed that the lack of nasal sensitivity persisted. Twelve out of fourteen of these subjects challenged with twice the NAR_{200} dose retained local desensitization to this increased dose and both subjects challenged with four times the NAR_{200} dose also showed no nasal response. Three of the subjects who failed to become desensitized immediately after the initial schedule were found to lack sensitivity to the NAR_{200} dose 6 weeks later, and two of the three failed to respond to twice this dose.

Table 3. Mean symptom scores following nasal challenge with the NAR_{200} dose of grass pollen extract

Group	Initial	Immediately post initial schedule	Approx. 6 weeks later
1 Lactose + allergen	4.4	2.9	1.2
2 DSCG + allergen	4.1	2.4	0.9
3 DSCG + saline	5.8	5.6	Not done
All desensitized	4.3	2.3	1.2
All non-desensitized	5.1	5.4	Not done

Twenty subjects who were locally desensitized to grass pollen extract were challenged with 1/5 dilutions of 'shrub' pollen extract (B1) and mixed tree pollen extract (B3). Nineteen of the twenty failed to respond by NAR increase to B1 challenge and only one of the twenty responded to B3 challenge. In order that previous nasal challenge with these two allergen mixtures should not interfere directly with nasal sensitivity by local desensitization, nasal sensitivity to these allergens had not been determined before the desensitizing schedule to grass pollen extract was carried out. Fourteen out of twenty, however, had positive weal and flare skin reactions greater than or equal to 4 mm weal diameter to B1 and fifteen out of twenty similar reactions to B3. Many, but by no means all, subjects who give such positive skin responses will normally respond to the dose of allergen extract used (1/5). Local desensitization against grass pollen would seem therefore, by implication, to have influenced nasal sensitivity to allergens other than grass pollens.

The symptom scores following NAR_{200} nasal challenge confirm that the local desensitization defined in terms of NAR responses is also reflected in symptom changes. Table 3 shows the mean symptom scores of the three groups before and after the initial schedule and approximately 6 weeks later. Also included are the symptom scores of subjects divided into desensitized and non-desensitized using the NAR criterion.

Thus, in desensitized subjects, not only does the NAR fail to increase on nasal challenge which reflects mainly a lack of mucosal oedema, but also the symptoms of sneezing and nasal discharge decrease in intensity. Of interest is the continued de-

crease in symptom score in the desensitized subjects during the 6 week period free of challenge. This suggests that local nasal desensitization is a continuing process once initiated.*

Table 4. Descriptive statistics for parameters recorded on diary cards

	Group 1	Group 2	Group 3
No. of subjects	11	12	10
Sneezing	23.9 ± 19.2	26.2 ± 18.5	41.9 ± 18.4
Nasal discharge	25.5 ± 19.1	26.4 ± 23.8	38.2 ± 24.6
Nasal obstruction	13.0 ± 17.0	13.2 ± 12.7	35.1 ± 26.2
Eye irritation and watering	26.4 ± 20.2	23.2 ± 11.8	39.9 ± 22.7
Antihistamine usage	13.1 ± 20.9	15.9 ± 15.8	27.7 ± 19.0
Throat irritation	7.5 ± 12.2	9.6 ± 9.1	14.3 ± 13.5
Breathlessness	2.2 ± 5.1	2.4 ± 3.1	4.6 ± 6.4
Wheezing	1.5 ± 3.9	4.2 ± 6.6	4.9 ± 8.5
Cough	2.9 ± 4.9	2.1 ± 3.3	14.0 ± 16.6

Results are mean and standard deviation of total score for whole 6 week period.

Table 5. Summary of significance tests for scores of parameters recorded on diary cards

	Comparison					
	Group 1 v Group 2		Group 1 v Group 3		Group 2 v Group 3	
	U	P	U	P	U	P
Sneezing	63.0	$P > 0.05$	27.0	$0.025 < P < 0.05$	33.5	$0.025 < P < 0.05$
Nasal discharge	62.0	$P > 0.05$	37.5	$P > 0.05$	43.0	$P > 0.05$
Nasal obstruction	58.5	$P > 0.05$	27.0	$0.025 < P < 0.05$	31.0	$0.025 < P < 0.05$
Eye irritation and watering	63.5	$P > 0.05$	34.0	$P > 0.05$	36.0	$P > 0.05$
Antihistamines	51.5	$P > 0.05$	20.0	$0.001 < P < 0.01$	38.0	$P > 0.05$
Throat irritation	45.0	$P > 0.05$	35.0	$P > 0.05$	50.5	$P > 0.05$
Breathlessness	49.5	$P > 0.05$	36.0	$P > 0.05$	50.5	$P > 0.05$
Wheezing	45.5	$P > 0.05$	46.5	$P > 0.05$	54.0	$P > 0.05$
Cough	65.0	$P > 0.05$	32.0	$P > 0.05$	35.0	$P > 0.05$

Clinical trial

A total of thirty-nine subjects who had been involved in the laboratory studies participated in the trial. This comprised twelve group 1 subjects (lactose + allergen), seventeen group 2 subjects (DSCG + allergen), and ten group 3 subjects (DSCG + saline). Diary cards from six subjects were incomplete and have been excluded from the analyses. The reasons given for incompleteness were varied but summer holidays abroad was the commonest. The diary cards analysed were provided by eleven group 1 (nine desensitized subjects), twelve group 2 (nine desensitized), and ten group 3

* Six out of six subjects who were re-challenged using the NAR₂₀₀ dose of grass pollen extract 1 year after being shown to be desensitized retained the desensitized state. In none did any NAR increases occur and the mean symptom score for the group was 0.17.

(one desensitized). The means and standard deviations of total scores for each parameter recorded on the diary cards over the whole 6 week period are presented in Table 4. The Mann Whitney U test was used to compare these data derived from the three groups. This analysis is presented in Table 5. In summary there appears to be no significant differences between groups 1 and 2 with respect to any parameter, whilst both sneezing and nasal obstruction scores were significantly less in these groups than in group 3. This is in spite of the fact that group 3 used significantly greater numbers of antihistamine tablets than group 1 and greater numbers, though not significantly so, than group 2. This comparison of groups does not reveal any significant difference in the incidence of lower respiratory tract symptoms, although these were relatively uncommon in all three groups.

Table 6. Comparison of scores of parameters recorded on the diary cards in desensitized and non-desensitized patients

Variable	Desensitized (nineteen patients)	Non-desensitized (fourteen patients)	Probability†
Sneezing	23.7 ± 17.9*	38.9 ± 19.4*	0.01 < P < 0.025
Nasal discharge	22.3 ± 19.3	39.6 ± 23.6	0.01 < P < 0.025
Nasal obstruction	12.4 ± 13.4	29.7 ± 25.7	0.025 < P < 0.05
Eye irritation and watering	21.3 ± 15.1	40.1 ± 19.5	0.001 < P < 0.01
Antihistamine consumption	15.1 ± 19.1	23.2 ± 18.7	0.025 < P < 0.05
Throat irritation	6.2 ± 6.9	21.1 ± 22.3	0.01 < P < 0.025
Breathlessness	2.9 ± 4.8	3.9 ± 5.5	P > 0.05
Wheezing	1.8 ± 4.0	5.8 ± 8.5	P > 0.05
Cough	2.4 ± 4.2	10.9 ± 14.8	0.025 < P < 0.05

* Values are mean ± SD.

† From Mann Whitney U test (one tailed).

As each group contained different proportions of desensitized and non-desensitized individuals, a direct comparison was made with the subjects divided according to the criterion of local desensitization already described and considering the subjects' nasal responsiveness before the pollen season. This analysis is shown in Table 6. Significant differences are demonstrated with respect to sneezing, nasal discharge, nasal obstruction, eye symptoms, antihistamine usage, throat irritation and cough. In each case the desensitized group scored significantly less.

Thus the clinical trial supports the laboratory data and also indicates that local nasal desensitization persists at least for several months. It also suggests that although the administration of the allergen extracts during the desensitizing schedule was to the nasal mucosa, significant loss of sensitivity also took place in the conjunctiva.

Discussion

Considerable reduction in bronchial reactivity was shown by Herxheimer (1951) and by Herxheimer & Prior (1952) following a series of small doses of aerosolized allergen. Their patients were demonstrated to be initially sensitive to a variety of allergens including pollens, moulds and house dust by bronchial challenge and bronchial sensitivity was shown by objective means to be appreciably diminished following a

number of challenges. They also claimed that in 27% of patients treated in this way asthmatic symptoms disappeared. In patients with both allergic rhinitis and allergic asthma Swineford *et al.* (1955) presented further evidence to suggest that clinically valuable reduction in local sensitivity could result from small graded doses of allergen presented locally to either the nasal mucosa or by oral inhalation. Since this time interest in changes in local responsiveness induced by local application of allergen appears to have waned. We were impressed by the persistence of local nasal desensitization in those subjects in whom it was 'accidentally' induced during the determination of the NAR_{200} dose of allergen and also by their statements that the expected summer symptoms had failed to occur. At this time it appeared likely from a retrospective study of previous results that application of allergen to the nasal mucosa whilst the local reaction was blocked by DSCG might facilitate local desensitization and hence this was investigated as well as the influence of repeated allergen challenge.

The laboratory results show that local responsiveness can be markedly reduced if a sufficient number of doses of allergen are administered. The number required varies from patient to patient, but is usually greater than four, and eight doses seems to be suitable for most. DSCG does not facilitate the induction of local desensitization nor does it, by itself, alter nasal reactivity in the long term. On the other hand, as it blocks the expected nasal response in approximately three-quarters of the subjects it renders the local desensitizing procedure very much more acceptable to patients.

The definition of local desensitization adopted—failure to increase NAR on allergen challenge—was intended to be as objective as possible. Using this criterion, local desensitization is associated with considerable reduction in the symptom response on nasal challenge. Thus sneezing and nasal discharge are also influenced as well as nasal obstruction. The decrease in nasal responsiveness was shown to persist when tests were carried out several weeks after induction. Not only was there a failure of the expected NAR response to challenge with the NAR_{200} dose of allergen but also with concentrations greater than this. In addition the symptom scores tended to decrease still further with the passage of this intervening period free of challenge. Thus the administration of several doses of allergen appears to initiate a process which, once triggered, not only persists, but becomes more effective.

Comparison of those subjects who received allergen either with or without DSCG and who developed local desensitization with those who did not, failed to indicate any obvious difference in history, age, sex or initial degree of either nasal or skin reactivity. Of the thirty-two subjects in groups 1 and 2 (receiving antigen) thirteen gave 'late' Arthus-like nasal reactions in addition to typical early reactions (Taylor & Shivalkar, 1971c). No difference in the incidence of local desensitization was noted when the subjects were grouped in this way. Of eight desensitized subjects who initially reacted by both early and late nasal responses, four lost both early and late reactivity when challenged after an intervening period whilst the others failed to respond by an early reaction but retained 'late' reactivity. It has been suggested by Pepys (1969) that the occurrence of type III (Arthus) reactivity is dependent on tissue changes brought about by a preceding type I reaction yet half of these latter patients suffered 'late' nasal reactions in the absence of an early response. This may either indicate that local nasal desensitization was incomplete and that minor type I changes took place in the nasal mucosa or that 'late' nasal reactivity is not typical of type III reactivity.

The specificity of local desensitization requires comment. In designing the protocol of the study, it was appreciated that in order to investigate the specificity of any

induced decrease in nasal responsiveness it would be ideal if the nasal sensitivity to allergens other than grass pollens was known. Yet this determination by nasal challenge might itself alter future nasal reactivity. A qualified reliance on skin sensitivity tests to other allergens was therefore accepted. A high proportion of subjects gave significant positive weal and flare skin responses to either one or both of extracts of 'mixed shrub' pollens (B1) or mixed tree pollens (B3). Of those responding on skin testing, only one of fourteen gave a positive nasal challenge test with B1 extract and one of fifteen with B3 extract after local desensitization to grass pollens. These findings may be interpreted in several ways.

1. In spite of skin reactivity to B1 or B3 the subjects did not possess nasal sensitivity to these allergens before local desensitization. Lack of nasal sensitivity in the presence of skin sensitivity is not uncommon in our experience, and may well account for the failure of some subjects to react. It is, however, very unlikely to account for lack of responsiveness in such a high proportion of subjects.

2. Local desensitization is not induced by specific immunological mechanisms. Many factors, both extrinsic and intrinsic, may influence local tissue responsiveness without exhibiting immunological specificity. The dependence of local desensitization on allergen administration, its long persistence, and the tendency for the efficiency of desensitization to increase with time without additional manipulations would, however, all point to an immunological mechanism being involved.

3. The range of pollens used may all share 'allergenic' determinants. Multiple skin sensitivity is the rule in the atopic state. Does this represent a proportion of identical molecules in diverse skin-test preparations, common determinants shared by non-identical molecules, or genuine primary sensitization to multiple different allergens? It is commonly considered that multiple sensitization is the explanation, and yet there is no firm evidence for this belief. Antigenic analysis of both grass pollens (Marsh & Haddad, 1958) and tree pollens (Segal, Kemp & Frick, 1970) have shown the existence of common antigenic determinants within each group. Unfortunately the relationship between antigenic determinants as demonstrated by rabbit antisera and allergenic determinants with which sensitized human tissues react is problematical. Berrens (1971) has made a determined effort to bring order out of chaos by suggesting that allergens form a distinct class of biologically active substances distinct in many ways from molecules which behave as antigens. He has provided evidence to suggest that the allergenic determinant may be a lysine-sugar unit, generated by Maillard type 'browning' reactions, with the specificity determined by nearby amino acids (Berrens, 1965). As many allergens do not appear to require an intact tertiary structure in order to possess activity, the range of size and conformation of allergenic determinants may be somewhat limited with consequent common cross-reactivity. We would favour the explanation of common allergenic determinants to account for the apparent blocking of responsiveness to tree and 'shrub' pollens by local desensitization against grass pollens.

There are a number of points at which the allergic reaction to grass pollen might be interrupted by immunological means. As the blocking effect observed was persistent, only those possibilities which would result in chronic change in reactivity will be considered. The mechanisms involved in the reduction in sensitivity resulting from conventional immunotherapy (hyposensitization) are as yet unclear. Although blocking antibody was first demonstrated many years ago (Cooke *et al.*, 1935) and has been the subject of considerable research, the evidence available would suggest that the

production of this antibody is not solely responsible for the change in reactivity. Blocking antibody, mainly residing in the IgG class, increases in concentration in serum with parenteral administration of allergen, but attempts to correlate clinical improvement with antibody levels have given conflicting results (Loveless, 1943; Arbesman *et al.*, 1960; Lichtenstein, Norman & Winkenwerder, 1969). Decrease in production of specific IgE and changes in effector cell response mechanisms have been suggested by Levy & Lichtenstein (1970) as other possible factors. The induction of specific tolerance in the T lymphocyte population with consequent lack of cell cooperation with B lymphocytes was raised by Brostoff & Roitt (1970) who demonstrated reduction of blast transformation against pollen after conventional hyposensitization. All these mechanisms involve changes in the reactivity of the whole individual. The changes we have observed appear to be limited to the nose and conjunctiva. Certainly, skin reactivity did not change, and there was no significant difference in the incidence of breathlessness and wheezing in the desensitized and undesensitized groups. It is likely, therefore, that mechanisms which are capable of changing local reactivity only are involved.

It has become increasingly recognized that local application of an antigen to a mucosal surface commonly results in the production of antibody of the IgA class which is found in its secretory form (SIgA) in mucus. This immunoglobulin is produced locally (Tomasi & Bienenstock, 1968; Tourville *et al.*, 1969) and the immune response may remain essentially localized to the site of antigen presentation (Centifanto, Little & Kaufman, 1970; Waldman *et al.*, 1970). Whilst the majority of studies on SIgA production have been concerned with the induction of immunity to infectious agents, the possibility that production of SIgA against allergens might be important in determining the outcome of an allergen challenge to sensitized tissue has been raised. Both Dolovich, Tomasi & Arbesman (1970) and Turk, Lichtenstein & Norman (1970) were able to demonstrate SIgA against ragweed pollen in nasal secretions. The latter workers showed that this antibody had the ability to block specifically the release of histamine from the allergen challenged leucocytes of ragweed sensitive individuals *in vitro*. They were able to demonstrate some anti-ragweed blocking activity in the nasal secretions of all subjects examined, including non-allergic controls. Although the mean blocking activity of nasal mucus from a group of patients treated by parenteral immunotherapy was significantly higher than that in a group receiving placebo injections, the scatter of results was such as to make interpretation difficult. In addition they could not show any correlation between symptom scores during the pollen season and the ability of nasal secretions to inhibit histamine release.

The evidence suggests that the production of SIgA is unlikely to contribute greatly to the clinical improvement derived from conventional parenteral immunotherapy. Parenteral immunization would not, however, be expected to influence greatly the local nasal production of specific SIgA. Local application to the nasal mucosa would be expected to lead to a far greater local SIgA response. The local production of specific SIgA induced by the local application of repeated doses of grass pollen extracts with the consequent blocking of access of the allergen to IgE sensitized cells is the most likely mechanism for the desensitization phenomenon observed. As SIgA has been shown to have rather less specificity than serum IgG (Waldman, Wigley & Small, 1969), this may also account in part for the relative lack of specificity of the desensitization observed.

One question which requires answer is why does this phenomenon not occur

commonly during exposure to allergens in everyday life with consequent spontaneous desensitization? The nature of the allergen preparation used, i.e. soluble rather than particulate, and the size and timing of doses may be important in this context. Further investigation is clearly required. The induction of local desensitization, which is a relatively quick and easy procedure and so far has been without complications, constitutes an alternative approach to the treatment of allergic rhinitis.

Acknowledgments

We wish to thank Mr Peter Mills for invaluable assistance with the statistical analysis and Messrs Fisons Pharmaceutical Division for financial support.

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