

Asthmatic Response Induced by Nasal Challenge with Allergen

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Key Words

Asthmatic response · Allergic rhinitis · Nasal allergy · Nasal challenge with allergens

Abstract

Background: There is a link between the upper and lower airways. Allergic rhinitis and bronchial asthma may coexist, but they can also affect each other. **Objective:** To investigate the possibility of nasal allergy being able to induce a secondary asthmatic response (AR). **Methods:** In 82 asthmatics responding insufficiently to standard antiasthmatic therapy and demonstrating negative ARs to bronchial challenge with allergen, 82 nasal challenges with various inhalant allergens were performed by means of rhinomanometry in combination with spirometry (vital capacity and forced expiratory volume in 1 s). In 33 control subjects suffering from allergic rhinitis (n = 18) or bronchial asthma (n = 15) only, 33 nasal challenges with inhalant allergens were performed by rhinomanometry and supplemented with spirometry. **Results:** Of the 82 nasal challenges, 69 produced a positive nasal response ($p < 0.01$) and 13 were negative ($p > 0.05$). In 58 cases with a positive nasal challenge, a secondarily induced AR was recorded ($p < 0.01$). The following types of ARs were documented: 17 isolated immediate ARs ($p < 0.01$), 24 isolated late ARs ($p < 0.01$), 12 dual late ARs (immediate + late, $p < 0.05$ and $p < 0.01$, respectively) and 5 isolated delayed ARs ($p < 0.05$). **Conclusions:** (1) An allergic reaction occurring initially in the nasal mucosa can play an important role in bronchial asthma by inducing a secondary AR, and (2) nasal challenge with allergen performed by rhinomanometry in

combination with lung function recording (e.g. spirometry) may then determine the possible need for additional intranasal antiallergic treatment and sparing of antiasthmatic drugs.

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Introduction

The link between allergic rhinitis and bronchial asthma and their mutual influence has been reported repeatedly in the literature [1–9]. Allergic rhinitis constitutes an important risk factor for new-onset bronchial asthma [1, 2, 9]. Allergic disorders of the upper airways may also have a remarkable impact on the immunologic processes in the lower airways [1–11]. The occurrence of concomitant rhinitis in patients with bronchial asthma has been detected in 19–80% of patients [2, 3, 7–11], whereas bronchial asthma may appear in 19–40% of patients with allergic rhinitis [3, 7, 9–12]. In this regard there is a need for reliable diagnostic parameters and procedures for clinical detection and confirmation of the possible involvement of the upper airways and nasal allergy in the lower airways, especially in patients suffering from bronchial asthma. The relationship between the allergy components of the upper and lower airways has been investigated from various perspectives [13–20]. These studies deal either with the immunologic aspects, such as the appearance and effects of various mediators, cytokines and other factors [13–18], with the appearance and migration of particular cell types in the blood, topical tissue or spu-

Table 1. Characteristics of the patients and control subjects

	Patients (n = 82)	Control subjects	
		group I (n = 18)	group II (n = 15)
Age, years	33 ± 7	31 ± 5	27 ± 6
Sex (M/F), n	38/44	8/10	7/8
Duration of BA, years	4.3 ± 1.5	0	5.5 ± 1.9
FEV ₁ , % predicted	97.8 ± 5.1	94.2 ± 8.8	91.5 ± 6.3
FVC, % predicted	98.0 ± 7.4	99.1 ± 4.2	95.6 ± 4.9
Blood eosinophil count, × 10 ⁶ /l ^a	408 ± 36	341 ± 23	515 ± 69
Bronchial histamine PD ₂₀ ^b , n			
≤4 mg/ml	0	0	9
8–32 mg/ml	81	3	6
>32 mg/ml	1	15	0
BPT positive/negative per patient, n	0/2–3	0/0	1–2/0–1

Values are means ± SD, except where indicated otherwise. Group I = Patients suffering only from allergic rhinitis; group II = patients suffering only from bronchial asthma; BA = bronchial asthma; FEV₁ = forced expiratory volume in 1 second; FVC = forced vital capacity; BPT = bronchial provocation test with allergen.

^a Normal value for blood eosinophil count: <300 × 10⁶/l.

^b Normal value of bronchial threshold for histamine: >32.0 mg/ml.

tum/nasal secretions [3, 5, 8, 9, 13, 17–20] or with the therapeutic effects of various drugs on the concomitant disorder [7, 15, 21]. Nevertheless, there is a dearth of information concerning the development of particular types of allergic reactions and the response in one organ induced by the allergic reaction occurring initially in the other organ (e.g. nose-bronchial tree) [22–27]. The purpose of this study was to investigate (1) the possible involvement of the nasal mucosa and nasal allergy in the asthmatic response (AR) and (2) the possible utilization of nasal challenge with allergen, combined with spirometry, in the diagnosis of bronchial asthma, especially of the forms responding insufficiently to standard antiasthmatic therapy.

Patients and Methods

Patients

This study included 82 patients (38 males and 44 females, 20–45 years of age) suffering from mild to moderate bronchial asthma for longer than 2 years, in whom standard antiasthmatic treatment (inhaled glucocorticosteroids and β_2 -sympathomimetics, sometimes combined with nedocromil sodium) had not resulted in satisfactory improvement.

These patients showed reversible bronchoconstriction alternating with symptom-free periods. Their pulmonary function did not demonstrate any restrictive changes and they did not have any chronic infections of the airways (table 1). None of them had

received immunotherapy or oral corticosteroids. Their asthmatic attacks, occurring 1–3 times a week, had additionally been treated with various inhaled β_2 -sympathomimetics.

All patients demonstrated distinctly positive intracutaneous tests with various inhaled allergens and increased blood eosinophilia (>300 × 10⁶/l). Their bronchial histamine threshold (PD₂₀) was slightly decreased (8.0–32.0 mg/ml; table 1).

Bronchial provocation tests (BPTs) with various skin-positive inhaled allergens performed by means of spirometry were negative in all patients (table 1). However, a detailed diagnostic procedure revealed a positive history for allergic rhinitis in all these patients and they all demonstrated violaceous and edematous nasal mucosa on rhinoscopy.

In these 82 patients, 82 nasal challenges (nasal provocations tests, NPTs) with various inhaled allergens were performed by means of rhinomanometry in combination with spirometry. If the study participant showed a prechallenge forced expiratory volume in 1 s (FEV₁) lower than 80% of his/her predicted value, no BPT or NPT was carried out on that day. All BPTs and NPTs were performed during hospitalization of the patients under standard conditions.

The wash-out period for inhaled glucocorticosteroids, long-acting H₁-receptor antagonists and long-acting β_2 -sympathomimetics was 4 weeks, for nedocromil sodium and disodium cromoglycate 2 weeks, for short-acting H₁-receptor antagonists 48 h, short-acting β_2 -sympathomimetics 6 h and incidentally used nasal α_2 -sympathomimetics at least 4 h prior to each NPT.

A short-acting β_2 -sympathomimetic in the form of inhaled aerosol in a single dose of 2 × 100 µg was used as a rescue therapy. The study was approved by the local ethical committee, and informed consent was obtained from all participants.

Allergens

Dialyzed and lyophilized allergen extracts (Allergopharma, Germany) were diluted in phosphate-buffered saline (PBS) and used for skin tests at a concentration of 100 BU/ml and for nasal challenges at concentrations of 1,000–5,000 BU/ml (table 2).

If indicated, higher dilutions of the allergen extracts were used both for the skin tests and for the nasal challenges.

Skin Tests

The intracutaneous tests were evaluated 20 min and 6, 12, 24, 36, 48, 72 and 96 h after the intradermal allergen injection. A skin wheal reaction (>7.5 mm in diameter) appearing within 20 min after injection was considered to be a positive immediate skin response, an infiltration occurring 6–12 (24) h later to be a late skin response and skin induration appearing later than 24 h, usually between 36–72 h, after the allergen injection, to be a delayed skin response [23, 26, 29, 32].

Nasal Provocation Tests

Nasal challenges with allergens were performed by means of rhinomanometry, which has already been described in our previous reports [22, 23, 26, 28]. The response of the nasal mucosa (i.e. nasal obstruction) was evaluated by means of nasopharynx-nos-tril pressure gradient (NPG) parameters, which is the pressure difference between the nasopharyngeal cavity and the external air, expressed in cm H₂O. The NPTs were performed according to the following schedule: (1) baseline values were recorded 0, 5 and 10 min before the challenge; (2) PBS control values were recorded

Table 2. Survey of the allergens used for nasal provocation tests

Allergen	Concentration, BU/ml	Total responses (n = 82)	Nasal response		Induced asthmatic response	
			positive (n = 69)	negative (n = 13)	positive (n = 58)	negative (n = 24)
<i>Dermatophagoides pteronyssinus</i>	1,000	17	15	2	12	5
<i>Dermatophagoides farinae</i>	1,000	4	4	0	3	1
Dog ¹	3,000	5	4	1	5	0
Cat ¹	2,000	11	10	1	11	0
Guinea pig ¹	2,000	2	1	1	1	1
Hamster ¹	2,000	1	1	0	1	0
Horse ¹	2,000	3	2	1	1	2
Parakeet feathers	3,000	1	1	0	1	0
<i>Aspergillus fumigatus</i>	1,000	1	1	0	1	0
Grass pollen mix I	1,000	25	22	3	15	10
Grass pollen mix II	1,000	6	5	1	3	3
Tree pollen mix	3,000	4	2	2	2	2
Weed pollen mix	3,000	2	1	1	2	0

Grass pollen mix I = *Dactylis glomerata*, *Lolium perenne*, *Phleum pratensis* and *Poa pratensis*. Grass pollen mix II = *Festuca pratensis*, *Holcus lanatus*, *Agrostis alba* and *Anthoxanthum odoratum*. Tree pollen mix = *Betula pendula*, *Corylus avellana*, *Juniperus communis* and *Salix alba*. Weed pollen mix = *Artemisia vulgaris*, *Plantago lanceolata*, *Rumex acetosa* and *Taraxacum officinale*.

¹ Danders = hairs and squamae.

0, 5 and 10 min after a 3-min application of PBS to the nasal mucosa of the nonintubated nasal cavity by means of a saturated wad of cotton wool on a nasal probe inserted under the concha media, and (3) postchallenge values were recorded after a 3-min challenge with a single dose of allergen, carried out in the same manner as the challenge with PBS, at 0, 5, 10, 20, 30, 45, 90 and 120 min, and subsequently every hour up to the 12th hour, and then every 2nd hour during the periods between the 24th and 38th and the 48th and 56th hour. The allergens used for the NPTs were chosen with respect to the disease history and positive skin tests of the patients (table 2). However, these allergens were unable to elicit any AR in BPTs. The nasal response (NR) was assessed to be positive when the mean postchallenge NPG values increased by at least 2.0 cm H₂O (mean $\pm$ SE 1.2 $\pm$ 0.3) [23, 26, 28] with respect to the mean baseline values, recorded for at least 3 consecutive time points. NPG changes recorded within 60 min after the allergen challenge were considered to be a positive immediate NR, those recorded within 4–12 h to be a positive late NR and changes measured later than 24 h to be a positive delayed NR.

Control Tests with PBS

The control nasal challenge with PBS was carried out in each patient according to the same schedule as that used for the NPT with allergen, but 2 days later.

Spirometry

The vital capacity and the FEV₁ were recorded by means of a spiograph (Model D-75, Lode, The Netherlands). FEV₁ was considered to be the basic parameter for the assessment of bronchial obstruction (i.e. AR). The spiographic values were recorded simultaneously with the recording of the NPG values, at the same time points. These values were evaluated as follows: (1) a decrease

in FEV₁ or both FEV₁ and vital capacity of less than 10% with respect to the baseline values was considered negative, from 10 to 20% as doubtful and 20% (PD₂₀) or more as positive; (2) a decrease in FEV₁ recorded for at least 3 consecutive time points after the allergen challenge was considered to be a positive AR, and (3) a decrease in FEV₁ values measured within 60 min after the allergen challenge was designated a positive immediate AR, that recorded within 4–12 h as a positive late AR and an FEV₁ decrease appearing later than 24 h, usually between 36 and 72 h, as a positive delayed AR [29–32].

Repeated Nasal Challenge with Allergen

In 17 patients, 17 nasal challenges with allergen inducing positive ARs (5 isolated immediate ARs, 10 isolated late ARs and 2 isolated delayed ARs), monitored by rhinomanometry and spirometry, were repeated 2 weeks later, to check the reproducibility of the techniques.

Control Groups

Two control groups of adults aged 20–45 years were also studied. One group consisted of 18 patients suffering only from allergic rhinitis, without bronchial complaints. The other group included 15 patients suffering only from bronchial asthma, without nasal complaints, and demonstrating an immediate AR to various inhalant allergens during BPTs.

In patients belonging to the first group, 18 nasal challenges with inhalant allergens producing a positive NR (6 immediate and 12 late NRs) were repeated and combined with the recording of the spirometric values. In patients belonging to the second group, 15 nasal challenges were performed with those inhalant allergens producing the immediate AR to bronchial challenge and supplemented with the recording of the spirometric values.

Table 3. Review of the particular types of NR and induced AR

	Induced AR type					negative
	isolated immediate	isolated late	dual late	isolated delayed	dual delayed	
Positive NR (n = 69)	17	24	12	5	0	11
Isolated immediate (n = 23)	15	1	2	2	0	3
Isolated late (n = 27)	2	19	2	1	0	3
Dual late (n = 9)	0	2	4	1	0	2
Isolated delayed (n = 7)	0	2	4	1	0	0
Dual delayed (n = 3)	0	0	0	0	0	3
Negative NR (n = 13)	0	0	0	0	0	13
A total of 82 nasal challenges were performed in 82 patients.						

Table 4. Survey of induced ARs with respect to the individual allergens

	Induced AR type					negative (n = 24)
	isolated immediate (n = 17)	isolated late (n = 24)	dual late (n = 12)	isolated delayed (n = 5)	dual delayed (n = 0)	
<i>Dermatophagoides pteronyssinus</i>	4	5	2	1	0	5
<i>Dermatophagoides farinae</i>	1	1	0	1	0	1
Dog	1	2	2	0	0	0
Cat	3	6	1	1	0	0
Guinea pig	0	1	0	0	0	1
Hamster	1	0	0	0	0	0
Horse	0	1	0	0	0	2
Parakeet feathers	0	1	0	0	0	0
<i>Aspergillus fumigatus</i>	0	1	0	0	0	0
Grass pollen mix I	5	4	4	2	0	10
Grass pollen mix II	1	0	2	0	0	3
Tree pollen mix	0	1	1	0	0	2
Weed pollen mix	1	1	0	0	0	0

A total of 82 nasal challenges were performed in 82 patients. For explanations of the allergens used, see the footnotes to table 2.

Statistical Analysis

The nasal as well as the bronchial responses were statistically evaluated by means of the generalized multivariate analysis of variance (MANOVA) model proposed by Potthoff and Roy [33] and presented by Timm [34]. The postchallenge values (NPG and FEV₁) were compared with the prechallenge baseline values and statistically evaluated.

The polynomials were fitted to the mean curves over time (6 time points within 120 min and 18 time points between 4 and 12, 24 and 38 and 46 and 62 h after the allergen challenge), and the appropriate hypotheses were tested by the modified MANOVA computerized system [35]. A p value <0.05 was considered to be statistically significant. Additionally, the mean values of the NPG changes and the mean values of the FEV₁ changes of the same type

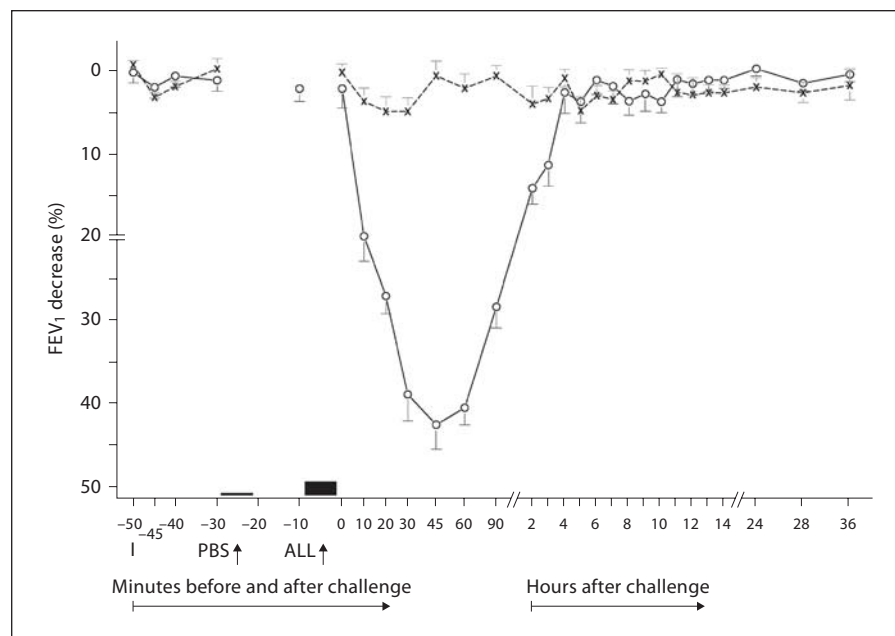
of response were compared with the mean values of the PBS control responses, at each of the recorded time points, and statistically evaluated by the Mann-Whitney U test. For these analyses also, a p value <0.05 was considered to be statistically significant.

Results

Nasal Responses

Of the 82 patients in whom 82 NPTs were performed, 69 patients developed 69 positive NRs (p < 0.01) and 13 patients demonstrated 13 negative NRs (p > 0.05). The

Fig. 1. The isolated immediate AR induced by nasal challenge with allergen. Shown are the mean percentage changes in the FEV₁ values calculated from 17 isolated immediate ARs (○) and 17 PBS control challenges (x). I = Initial values; ALL = allergen challenge. Data represent means $\pm$ SEM.



following types of positive NRs were recorded: 23 isolated immediate NRs ($p < 0.01$), 27 isolated late NRs ($p < 0.01$), 9 dual late NRs (immediate + late, $p < 0.05$ and $p < 0.01$, respectively), 7 isolated delayed NRs ($p < 0.01$) and 3 dual delayed NRs (immediate + delayed, $p < 0.01$ and $p < 0.05$, respectively; tables 2, 3). The 82 PBS control challenges did not induce any significant changes in the NPG values ($p > 0.1$). The differences in NPG values between the positive and negative NRs were statistically significant ($p < 0.01$).

No differences in the NRs were found with respect to the particular allergens used (tables 2, 4).

Asthmatic Responses

In 58 patients, 58 positive NRs (19 isolated immediate NRs, 26 isolated late NRs, 8 dual late NRs and 5 isolated delayed NRs) were accompanied by significantly positive ARs ($p < 0.01$). The following types of ARs were recorded: 17 isolated immediate ARs ($p < 0.01$; fig. 1), 24 isolated late ARs ($p < 0.01$; fig. 2), 12 dual late ARs (immediate + late, $p < 0.05$ and $p < 0.01$, respectively) and 5 isolated delayed ARs ($p < 0.05$; fig. 3). The remaining 24 patients, 11 of them displaying a positive NR and 13 demonstrating a negative NR, did not develop any AR ($p > 0.1$). No significant changes in the FEV₁ values were measured during the 82 PBS control tests ($p > 0.1$).

The distribution of the particular AR types is presented in table 3.

Repeated Nasal Challenge with Allergen

Seventeen positive NRs (5 isolated immediate NRs, 10 isolated late NRs and 2 isolated delayed NRs) recorded in 17 patients after repeated NPTs did not differ significantly from the first measured responses ($p > 0.2$).

The 17 induced ARs (5 immediate ARs, 10 late ARs and 2 delayed ARs) recorded in 17 patients after repeated NPTs did not demonstrate any significant differences with respect to the induced ARs measured after the first NPTs ($p > 0.1$).

Control Subjects

Of the 18 patients with allergic rhinitis only, 6 developed positive immediate and 12 late NRs ($p < 0.01$) during the repeated NPTs. None of these NRs was accompanied by significant changes in the FEV₁ values ($p > 0.1$).

The 15 patients with bronchial asthma only did not demonstrate any positive NR ($p > 0.05$) or significant changes in the FEV₁ values ($p > 0.1$) during the 15 NPTs.

Discussion

The upper and lower airways, both being parts of one respiratory system, have a number of features in common, but they also have a number of differences. The similar features concern the anatomical structures and physiologic functions, such as pseudostratified ciliated co-

Fig. 2. The isolated late AR induced by nasal challenge with allergen. Shown are the mean percentage changes in the FEV₁ values calculated from 24 isolated late ARs (Δ) and 24 PBS control challenges (x). I = Initial values; ALL = allergen challenge. Data represent means $\pm$ SEM.

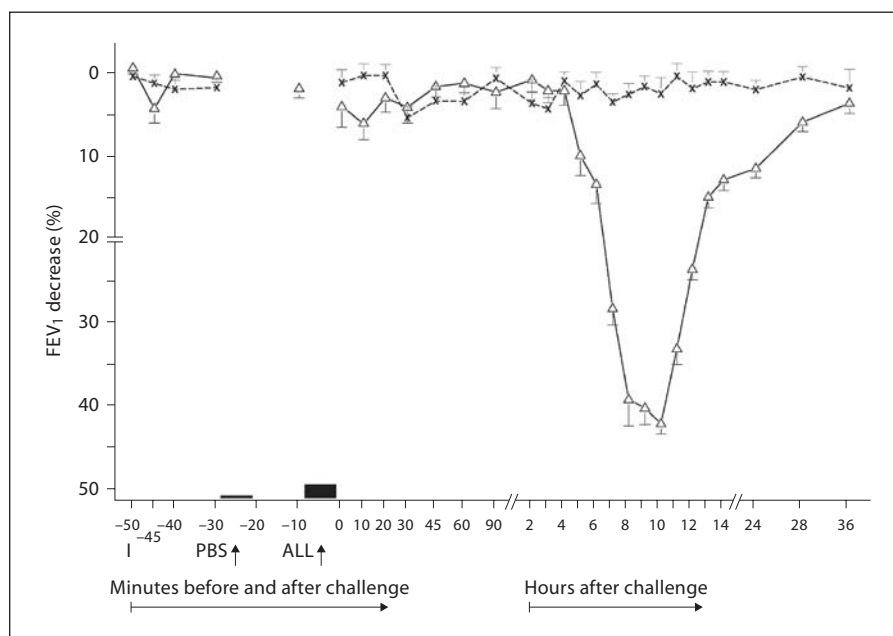
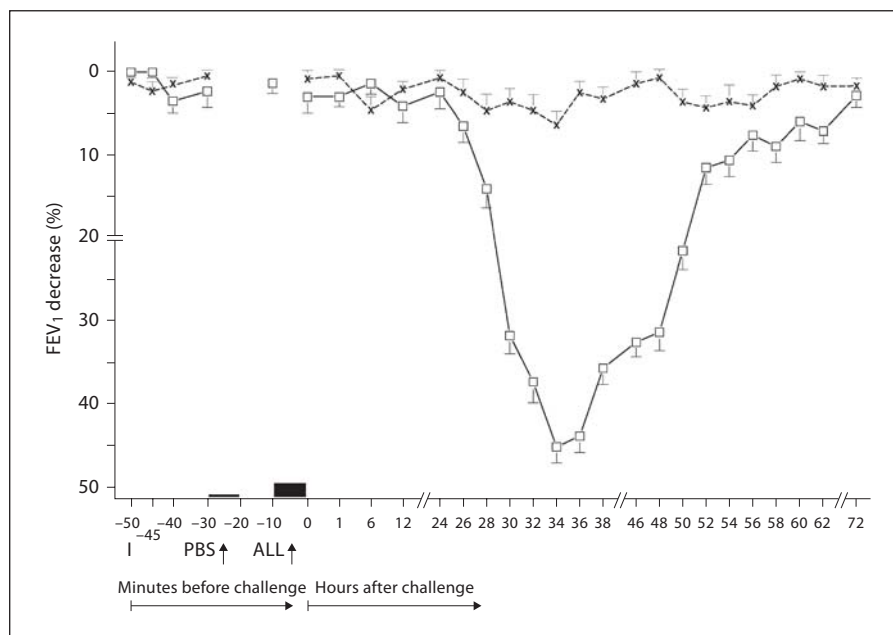


Fig. 3. The isolated delayed AR induced by nasal challenge with allergen. Shown are the mean percentage changes in the FEV₁ values calculated from 5 isolated delayed ARs ($\square$) and 5 PBS control challenges (x). I = Initial values; ALL = allergen challenge. Data represent means $\pm$ SEM.



luminal epithelium, an abundant capillary network, a relatively high number of mucosal glands, a rich nervous network and the presence of various cell types, e.g. mucosal mast cells and macrophages.

The differences between the upper and lower airways include the following: (1) the different localization and function – the nose serves as an entrance for the inspired air and the passageway for this air, which is also filtered

and conditioned there, whereas the lower airways are the end organ, whose most important function is gas exchange; (2) the presence of smooth muscles in the bronchial tree facilitating bronchoconstriction, which are lacking in the nose; (3) the presence of goblet cells in the nasal mucosa, which are absent in the bronchial tree; (4) the more frequent occurrence of mucosal edema in the nose than in the bronchial tree, and (5) the alternative

routes for inspired and exhaled air. In the case of distinct nasal obstruction, the necessary air can be managed through the mouth, whereas no comparable mechanism exists for the constricted bronchial tree [1, 2, 5, 6, 8, 10, 11].

The functional relationship between the upper and lower airways can be realized by means of various mechanisms [1–3, 5, 7–12, 16, 19]. The following mechanisms have been suggested in the literature: (1) the nasobronchial reflex [1–3, 8–11, 16, 19]; (2) altered breathing pattern [2, 3, 7, 12]; (3) postnasal drip [8, 9, 11, 12, 19]; (4) pulmonary aspiration of nasal secretions [1, 2, 7, 10, 12]; (5) uptake of various cytokines, mediators and adhesive molecules released or secreted in one organ into the particular transport medium (the blood circulation or secretions) and their subsequent delivery to the other organ [3, 5, 8, 9, 11, 17, 36]; (6) the neurogenic mechanism, including stimulation of the appropriate nerves and transfer of the neurokinins [7, 9, 16], and (7) stimulation and increase as well as inhibition and decrease of the count and function of various kinds of cells, followed by their subsequent migration and accumulation in the relevant tissue, mostly the mucosal membrane [3, 5, 8, 9, 17, 19].

Studies of the relationship between the upper and lower airways in human subjects by means of the challenge technique are not numerous [8, 9, 11, 13, 17, 18, 21–23, 36–40], and those using challenge with allergen are but few [8, 13, 17, 18, 21–23, 36–40]. In some of these studies, the effects of nasal challenge with allergen on the bronchial responsiveness to histamine/methacholine have been investigated [18, 37, 38]. Other studies have dealt with possible effects of bronchial challenge with allergen on nasal patency [39]. Nevertheless, the exact mechanisms underlying the relationship between the allergic component in the nasal mucosa and that in the bronchial tree have not yet been fully clarified [2–6, 9–11].

Our results may suggest a prominent role of the systemic route by which the nasal inflammation components, such as mediators, cytokines and other factors, as well as various kinds of cells, such as eosinophils, T lymphocytes and basophils, activated in the nasal mucosa stimulated by allergen, might propagate into the lower airways and affect them.

The possible involvement of the systemic route/pathways, by which various immunologic components and cells activated and stimulated in the nasal mucosa would propagate and migrate into the lower airways, is supported by the results of our preliminary pilot studies [22, 27]. In a group of comparable patients, treatment of patients with intranasally administered drugs prior to the nasal

challenges with allergen significantly prevented development of the secondarily induced ARs [27]. In another group of similar patients, introduction of long-term intranasal treatment significantly reduced bronchial complaints (asthmatic attacks due to bronchoconstriction), leading finally to decreased use of antiasthmatic drugs, both the glucocorticosteroids and the β_2 -sympathomimetics, with regard to both daily dose and frequency [22].

Our results also demonstrate the existence of an AR induced by the hypersensitivity mechanisms appearing primarily in the nasal mucosa due to stimulation by an allergen. The existence of various types of the secondarily induced AR is suggestive of the involvement of different hypersensitivity mechanisms.

The particular types of the secondarily induced AR are similar to the individual types of the primary AR due to bronchial challenge with allergen previously reported by us [29–32]. Similar types of NR have also been recorded after nasal challenge with allergen [23, 26, 28].

The results of our study are not fully comparable with the other authors' findings for several reasons. In most of the other studies, the effects of intranasally administered allergens on the responsiveness of the bronchial tree to inhaled histamine or methacholine were investigated [18, 37, 38]. In our study, we followed the effects of the nasal challenge with allergen directly on the bronchial tree and its ability to induce AR. We also followed the propagation of the allergic reaction from the nasal mucosa to the lower airways. This is a substantial difference, since the responsiveness of the airways to nonspecific agents such as histamine or methacholine on the one hand and to specific allergens on the other hand represent 2 different mechanisms [23, 29, 30]. These different mechanisms cannot be simply compared. However, they may exist together in the same organ [23, 29, 30]. Additional differences between the other investigators' studies and our study concern the study design, such as small numbers of patients [13, 25, 37], selection of the patients, who did not represent a homogenous group in every case, and monitoring of the NR to the allergen challenge, which was not always performed using an objective technique such as rhinomanometry [13, 25, 37].

Our data demonstrating the existence of the AR induced by the allergic reaction originating initially in the nasal mucosa disagree with the findings of some investigators who were unable to confirm this clinical phenomenon [38, 40]. Another interesting aspect of our observations is the recording of various types of the secondarily induced AR which were not unavoidably associated with

the NR. Moreover, the particular types of the induced AR did not correspond fully with the particular types of the NR appearing initially in the nasal mucosa. This fact would again suggest the manifold features of the allergic reaction and its particular types, its manifold effects upon various conditions in various organs and diversity in participation of the particular components of the immunologic system. Nevertheless, further concurrent clinical and immunologic research will be necessary to clarify the mechanisms underlying the particular types of the secondarily induced AR.

It can be concluded that confirmation of the involvement of nasal allergy in bronchial asthma in some patients by means of nasal challenges with allergen, monitored by rhinomanometry and spirometry, would motivate the need for additional treatment of nasal allergy. This treatment would then reduce or even prevent the secondarily induced AR and also decrease the requirement for antiasthmatic drugs.

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