

Nasal Smear as a Screening Test for Immediate-Type Nasal Allergy

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From a previous sample of 634 students and school children, 115 subjects were selected for a thorough rhinological examination and allergy work-up in order to assess the value of nasal secretion eosinophilia in screening for immediate-type nasal allergy. Part of the subjects had, in the previous study, been found to have secretion eosinophilia and a history of chronic/allergic rhinitis, part of the subjects had either a secretion eosinophilia or a rhinitis history, and part of them had neither a secretion eosinophilia nor a rhinitis history. A significant correlation was obtained between secretion eosinophilia and allergy. Nasal provocation tests correlated with skin tests in 87%, whereas the correlation between nasal provocation tests and IgE determinations in the serum was poorer. Thickening of the maxillary sinus was, when present, usually attributable to infection and not to allergy. Reasons for "false positive or false negative" smears for eosinophils are discussed.

Key words: atopic rhinitis; common allergens in rhinitis; immediate nasal allergy; nasal secretion eosinophilia.

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The clinical aspects of immediate-type nasal allergy are fairly well understood today. In the Nordic countries, birch, grass and mugwort pollens are responsible for the majority of seasonal symptoms, from which predominantly younger age groups seem to suffer, whereas house dust and, as a consequence, perennial symptoms become prominent in older age groups (12, 13).

This IgE-mediated, mucosal hypersensitivity is characterized by immediate skin reactivity to common allergens (23). Antigen-antibody reactions in the nasal mucosa cause eosinophil chemotactic agents to be released, probably from mast cells (22, 24). These chemotactic factors attract eosinophils to the reaction site and eosinophils are therefore regularly found in nasal secretion samples from patients presenting with symptoms of immediate nasal allergy (19, 29).

Nasal secretion eosinophilia is, however, also seen in nasal affections in which the mechanism is obscure, e.g. in "vasomotor rhinitis" (29), in nasal polyposis with intrinsic, non-atopic rhinitis, in rhinitis due to ASA intolerance (11), and in rhinitis caused by food allergens (4). Even in non-allergic persons, eosinophils can be found in the nasal secretion during acute viral infection in the nose (4, 10).

The present study forms a sequel to a previous investigation of the prevalence of rhinitis symptoms and the occurrence of nasal secretion eosinophilia in a random sample of 634 school children and university students (16). Selected groups of these students and children were subjected to a thorough rhinological examination and allergy evaluation in order to ascertain whether the test for nasal secretion eosinophilia was a reliable screening method for immediate-type nasal

allergy. At the same time, the relevance of clinical findings and tests used in the allergy evaluation was given special consideration.

MATERIAL AND METHODS

Material

For a previous survey of allergic rhinitis prevalence and occurrence of nasal secretion eosinophilia, a random sample of 634 school children and university students was collected (16). This material was divided into six groups on the basis of rhinitis history and presence of secretion eosinophilia. For the present allergy evaluation, about 20 subjects were randomly chosen from each of the six groups. The material of this study thus comprises 115 subjects, 55 females and 60 males. The groups, which consist of about equally many students and school children, are presented in Table 1A. The mean age of the 57 school children was 7.9 years (range 7–10 years), and the mean age of the 58 students 24.0 years (range 19–35 years).

Methods

1. A detailed questionnaire concerning history of allergy was filled out under the supervision of the skin testing technician and double-

checked by the authors. It will be referred to below as the "emphasized" case history.

2. Nasal appearance was examined by anterior and posterior rhinoscopy. Special attention was directed to occurrence of nasal secretion, changes in the mucosa of the conchae, and size of the pharyngeal tonsil, if present.

3. Sinus X-ray films (occipitontal and lateral views) were taken in 109 subjects in order to disclose sinus inflammations and obstructive adenoids. The maxillary sinuses were considered normal if no or only slight mucosal thickening (<1 mm) was present. The pharyngeal tonsil was considered normal in children when it filled not more than a third of the choanal opening. In students, a visible adenoid was regarded as an abnormal finding.

4. A blood sample was drawn in 104 subjects for blood eosinophil count. A count of $0.4 \times 10^9/l$ or higher was considered raised.

5. Skin testing to map out immediate hypersensitivity was performed by the prick technique with 15 common allergens: birch, willow, timothy, meadow foxtail, mugwort, orchard grass, house dust, house dust mite, cat, cow, dog, horse, sheep wool, *Alternaria* and *Cladosporium*. All antigen solutions, except those of pollens, contained 50% glycerol as a preservative. These solutions are used in routine provocative testing at the Department of Otolaryngology, Helsinki University Central Hospital. They are commercial solutions manufactured by Dome*. As control solutions, 1% histamine and glycerosaline were used. A test result was considered positive if the mean weal diameter was 3.0 mm or more, and doubtful if the diameter was 1–2.9 mm. Smaller reactions were regarded as negative (26).

6. Nasal provocation tests were performed to demonstrate dominant nasal allergy. The provocation was only qualitative. Dome's antigen solutions for provocation tests were used and the antigen vials were the same as

Table 1

Rhinitis history and nasal secretion eosinophilia in subjects included in the clinical allergy work-up: A=when entering the study. B=after checked case history

Rhinitis history	A		B	
	Smear eosinophilia +	Smear eosinophilia -	Smear eosinophilia +	Smear eosinophilia -
Allergic rhinitis	20	17	29	21
Chronic rhinitis	18	19	18	17
No rhinitis	21	20	12	18
Total	59	56	59	56

* The meadow foxtail solution was manufactured by Allergologisk Laboratorium A/S.

those used in the preceding skin tests. The provocation method and criteria for positivity have been reported earlier (17). A control provocation with glycerosaline solution was done prior to applying the first antigen. The nasal mucosa was first challenged with antigens which had elicited positive reactions on skin testing and then with antigens which could be suspected from history, and if there was still no positive reaction, house dust, house dust mite, *Cladosporium* or *Alternaria* was tested before the provocation was considered negative. The subjects did not know which antigen was tested.

7. Specific IgE in the serum was determined by RAST (Phadebas® RAST, Pharmacia Diagnostics Ab, Sweden), and the tests were performed in the Allergy Hospital of Helsinki University. All antigens which elicited positive nasal reactions or gave discordant results on skin testing and nasal challenge were tested by RAST. A score of 1–4 was regarded as a positive result.

The criteria for presence of immediate-type nasal allergy were as follows: 1) a positive skin test reaction confirmed by a history of rhinitis, 2) a positive nasal provocation result, or 3) a definite history of immediate nasal reaction to specified irritants with known allergenic potency (e.g. textiles, pet birds). Subjects were regarded as having active nasal symptoms at the time when the nasal smear was taken if they replied affirmatively to the question "Are you suffering from nasal symptoms at the present moment?" in the primary survey-questionnaire, or if secretion was seen by rhinoscopy when the smear was taken. Subjects who met neither criterion were included in the "inactive group".

RESULTS

History

In the group of subjects who at the outset had been classified as having no chronic or allergic rhinitis complaints, 12 out of 41 were, on closer scrutiny of the history, found to have had rhinitis symptoms (7 subjects allergic rhinitis

and 5 subjects chronic rhinitis). In the group of subjects who had given a history of chronic rhinitis, additional information in the "emphasized questionnaire" revealed that the symptoms were of allergic origin in six out of 37 subjects. The material is grouped according to the additional information in Table 1B.

Clinical findings

Thickening of the maxillary sinus mucosa correlated significantly with secretion, as observed by rhinoscopy ($\chi^2 = 10.15$, $P < 0.01$) but not with swelling of the nasal mucosa. Radiological sinus findings did not correlate with rhinitis history ($P > 0.05$), secretion eosinophilia ($P > 0.05$) or documented immediate-type nasal allergy ($P > 0.05$), although in the student group 12 out of 14 pathological sinus findings were made in subjects with immediate nasal allergy. When pathological sinus changes and nasal secretion neutrophilia were compared, a good correlation was revealed (Table 2).

Table 2
Correlation between pathological changes in the maxillary sinus mucosa and nasal secretion neutrophilia

Mucosal changes	Nasal + + +	smear + +	neutrophilia +	neutrophilia -	Total
Present	16	22	13	4	55
Absent	7	15	23	9	54
χ^2 (df=1)	7.75				
P	<0.01				

Adenoidectomy had been performed on 18 of the children with chronic or allergic rhinitis history, and also on two children in the group with no rhinitis history.

Results of tests for immediate allergy

Blood eosinophilia was present in only six out of 51 subjects whose nasal smears were positive for eosinophils and in two out of 53 with negative smears. All eight had immediate nasal allergy, seven of them also a history of eczema.

In skin tests, multiple reactions were common. Only six subjects showed a single positive reaction. The commonest allergens in the student group were mugwort ($n=10$), house dust ($n=9$), house dust mite ($n=9$), and birch ($n=7$). In the group of school children, pollens and animal danders were the most frequent: birch ($n=15$), orchard grass ($n=10$), cat ($n=10$), timothy ($n=8$), while only three positive house dust reactions were recorded.

A total of 254 nasal provocations were performed, 58 of them yielding positive results. Nasal provocation and skin test results were concordant in 87% (153 out of 175, not including doubtful reactions) and discordant in 13%. The nasal test was positive in 12 instances in which the corresponding skin test was negative and in 11 instances a positive skin test result was accompanied by a negative nasal test. The control provocation with the diluent, containing 50% glycerol, elicited a slight reaction on the nasal mucosa in 45 out of 115 subjects. A slight amount of secretion was seen to accumulate around the cotton wool pledget. In antigen provocation tests, a similar reaction was considered negative, and the reaction had to be markedly stronger before it was considered positive or even doubtful.

RAST did not yield a positive result in any instance in which the corresponding skin test and nasal challenge were negative but the reverse, a negative RAST result despite a positive skin or nasal test result, was not uncommon (Table 3).

There was a significant correlation between

Table 3
Correlation between RAST results and results of nasal provocation and skin tests

RAST	Nasal provocation result ($n=100$)			Skin test result ($n=141$)		
	+	+	-	+	+	-
Pos.	17	5	3	36	5	1
Neg.	26	28	21	23	19	57

Table 4

Correlation between secretion eosinophilia and results of skin tests and nasal provocation

Nasal smear	Skin test and/or nasal provocation		
	Positive	Doubtful	Negative
Eosinophilia ($n=59$)	36	16	7
No eosinophilia ($n=56$)	20	16	20
χ^2 (df=2)	9.38		
P	<0.01		

nasal secretion eosinophilia and immediate-type nasal allergy as demonstrated by skin testing or nasal provocation (Table 4).

Four subjects with secretion eosinophilia but negative skin tests and nasal provocation had a definite history of immediate nasal symptoms from allergens which were not included in the antigen set used in the tests. Ten subjects whose nasal smears showed no secretion eosinophilia but who had positive reactions on challenge or skin testing were sensitive to allergens which were out of season, and another six subjects with negative smears had no subjective or objective symptoms at the time when the smear was taken. When the subjects with doubtful reactions on skin testing and/or nasal challenge were excluded and the subjects regrouped according to presence or absence of active symptoms of nasal allergy, the correlation between secretion eosinophilia and active, immediate nasal allergy reached a highly significant level (Table 5). All three "false positive" smears showed neutrophils.

DISCUSSION

The purpose of the study was to evaluate the usefulness of the nasal smear as a screening test for immediate-type nasal allergy. The material was selected in regard to history of rhinitis, secretion eosinophilia and age. In the selected subjects, the capacity for immediate-type nasal reactions was ascertained by means

Table 5

Correlation between secretion eosinophilia and evidence of active allergic rhinitis (32 subjects with doubtful reactions excluded)

Nasal smear	Symptoms of active nasal allergy	
	Present	Absent
Eosinophilia (<i>n</i> = 43)	40	3
No eosinophilia (<i>n</i> = 40)	4	36
χ^2 (df = 1)	54.10	
<i>P</i>	< 0.001	

of routine tests for immediate, atopic allergy (23). Attempts were not made to find other possible forms of allergy or to identify the specific allergens to which the presence of eosinophils could be attributed.

This material illustrates the importance of taking a careful history, as the comprehensive "emphasized" case history revealed more allergic symptoms than did the questionnaire used in the primary survey.

Nasal allergy history and secretion eosinophilia have been shown to correlate with swelling of the nasal mucosa and secretion in the nose (16, 20). The majority of pathological changes in the sinus mucosa were seen in children (41 out of 55). In the total material, the findings in the maxillary sinus mucosa did not correlate significantly with history of nasal allergy, documented immediate-type nasal allergy or nasal secretion eosinophilia. Sinus findings did, however, correlate significantly with nasal hypersecretion and increased numbers of neutrophils and it may be assumed that thickening of the sinus mucosa was mostly due to infection, and not to allergy. Only in the student group did mucosal thickening occur mainly in subjects with documented nasal allergy but the correlation was not significant owing to the fact that the total number of positive findings was small in the student group.

Blood eosinophilia seemed to have little diagnostic value in the nasal allergy evalu-

ation. This observation has also been made in other studies (21).

The skin test results obtained in this material agree with results reported earlier (12, 13) in that pollen allergies dominated in the school children, while house dust and house dust mite reactions were more common in the student group. It should be noted that the positive skin reactions in the present material were not all confirmed by nasal provocation.

RAST yielded negative results in many instances in which skin tests and nasal provocation tests had been positive (Table 4). This may perhaps be explained by a local production of IgE (14, 18, 27). In studies in which IgE determinations were made from the nasal secretion, a higher correlation between RAST and nasal provocation results has been demonstrated (7). Organ specificity in allergy has been emphasized by several authors (1, 3, 8, 25).

Nasal provocation should be performed when other data are contradictory or doubtful (2, 5, 6, 15). However, provocative testing has not attained optimal reliability, partly because the antigen solutions are not yet standardized and also because the solutions may contain nonspecific irritants (2, 9). The nonspecific reactions elicited by the control solutions used in this study were mild and did not, as a rule, cause difficulties in the interpretation, as the antigen provocation was only qualitative. In quantitative provocation, which calls for alert observation of the slightest symptoms, unspecific reactions may be misleading.

In the three cases of "false positive" secretion eosinophilia (Table 5), eosinophilia occurred in combination with secretion neutrophilia, and neutrophils were also found in three out of four smears which were "false negative" for eosinophils. Infection may cause small numbers of eosinophils to appear in the nasal secretion of non-allergic persons. Conversely, it may also cause a temporary disappearance of eosinophils from the secretion of persons with allergic rhinitis (4, 10). However, it should be borne in mind that the

present allergy evaluation did not set out to reveal all forms of allergy which could account for the secretion eosinophilia. In the "false negative" smears, the absence of eosinophils could also be due to the uneven distribution of eosinophils in the nasal mucosa (28) and in the secretion (10). Thus marked neutrophilia (infection) in combination with eosinophilia or a suspicion that the smear may be "false negative" is an indication for taking a second nasal sample, and many smears may be necessary in doubtful cases.

Secretion eosinophilia was found to correlate highly significantly with active immediate-type nasal allergy (Table 5), which is important from the standpoint of clinical work. In the whole material, the correlation between nasal secretion eosinophilia and immediate-type allergy as demonstrated by skin tests and nasal provocation reached a significant level, which supports the view that, at least in younger age groups, the nasal smear is a useful screening test for nasal allergy.

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