

Hyposmia in allergic rhinitis

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Background: The association between nasal allergy and loss or diminution of smell is frequently alluded to in the literature; however, neither the true prevalence of hyposmia in individuals with allergic rhinitis nor its bases have been established.

Methods: We assessed olfactory threshold for phenylethyl alcohol in 91 patients with symptoms of allergic rhinitis and 80 nonatopic control subjects. To determine the degree to which nasal congestion contributes to hyposmia in allergic rhinitis, total nasal resistance was measured in 64 of the patients and 72 of the control subjects.

Results: Olfactory thresholds were significantly higher in allergic patients than in control subjects ($p < 0.001$), with 23.1% of the patients demonstrating a clinically significant smell loss (defined as threshold at or above the 2.5th percentile of control values). Although nasal resistance was significantly higher among patients than among controls ($p < 0.001$), it was not related to olfactory threshold in either group. Clinical or radiographic evidence of sinusitis or nasal polyps or both in allergy patients was found to be significantly associated with hyposmia ($p < 0.006$).

Conclusions: The observed prevalence of hyposmia among patients with allergic rhinitis suggests that this is a major etiologic factor contributing to smell disorders. Sinusitis or nasal polyps or both may underlie many cases of allergy-related hyposmia. (*J ALLERGY CLIN IMMUNOL* 1993;91:747-51.)

Key words: Hyposmia, nasal resistance, allergic rhinitis, olfaction, sinusitis, nasal polyps

An association between nasal allergy and loss or diminution of smell has been noted frequently in the literature.¹⁻⁵ This problem is generally assumed to result primarily from nasal obstruction,⁵ although other mechanisms associated with the allergic process may play a role. For example, Church et al.⁶ observed marked histopathologic changes in the nasal mucous membrane of hyposmic patients with nasal allergies, raising the possibility that destruction of the mucosa, or processes leading to such destruction, may contribute to allergy-related olfactory loss. Little objective information is available on the prevalence of hyposmia among nasal allergy sufferers, however, and none is available on the role of nasal patency in allergy-related hyposmia.

Only one study, reported in abstract form, has specifically assessed olfactory function in allergy patients. Seiden et al.⁷ administered an odor identification test to 34 patients with allergic rhinitis (AR)

Abbreviations used

AR:	Allergic rhinitis
NSD:	Nasal-sinus disease (sinusitis or nasal polyps or both)
Pa:	Pascal
PEA:	Phenylethyl alcohol
TNR:	Total nasal airway resistance

and found 35.3% had measurable smell loss; moreover, 58.5% indicated that they had experienced smell problems. AR is estimated to affect 10% to 15% of the general population.^{8,9} Thus should the finding of such a high prevalence of hyposmia in these patients be verified in a larger study, nasal allergy could represent the single most common etiologic factor in olfactory dysfunction.

The present study was designed to assess olfactory function in patients with signs and symptoms of nasal allergy, and to delineate the relationship between smell acuity and nasal patency in this clinical population.

METHODS

Subjects

Patients included 91 persons (31 males, 60 females) between the ages of 8 and 56 years (mean, 29.5 years) who came to an outpatient allergy practice for evaluation of nasal symptoms. A history consistent with nasal allergic symp-

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toms was sought from each, and each underwent intradermal skin testing with a battery of allergens including house dust mites, ragweed, grass mix, tree mix, five molds, English plantain, and dog and cat dander. Reactions were scored 0 to 4+, with use of accepted criteria.¹⁰ AR was diagnosed on the basis of the following: (1) a current history of sneezing, pruritus of the eyes, nose, or palate, or nasal congestion (i.e., all patients were symptomatic at the time of their participation in the study); and (2) one or more positive skin tests. Positive skin tests were consistent with patient reports of seasonal or perennial allergic symptoms.

All patients underwent examination of the nasal cavity by anterior rhinoscopy; 18 were referred on the basis of presenting symptomatology for imaging of the paranasal sinuses (11 by computerized tomography, 7 by radiography). Nasal polyps were diagnosed in 10 patients; 24 patients (including 6 in whom polyps were observed) were diagnosed as having sinusitis on the basis of physical findings or imaging results or both. It is possible that not all cases of nasal polyps or sinusitis were diagnosed, but the relatively high observed prevalence of one or both of these conditions suggests that diagnostic procedures were reasonably rigorous.

Control subjects were 27 male and 53 female volunteers without history or symptoms of rhinitis, ranging in age from 20 to 59 years (mean, 29.4 years). Control and patient groups did not differ significantly in age or gender distribution.

This study was approved by the Institutional Review Board of Thomas Jefferson University. All subjects gave informed consent for participation.

Questionnaire

Patients and control subjects completed a brief questionnaire that elicited information concerning allergy symptoms, current medications, and any history of olfactory difficulties.

Olfactory assessment

Detection threshold for the odorant phenylethyl alcohol (PEA) was obtained as the measure of absolute olfactory sensitivity. Unlike most odorous substances, this volatile appears to stimulate the olfactory system exclusively (i.e., it elicits little or no nasal trigeminal response at any concentration),^{11, 12} and it is used for clinical assessment of olfactory function in two of the five, National Institutes of Health-funded Chemosensory Clinical Research Centers.^{13, 14} A threshold rather than an odor identification measure was chosen because this is less likely to be confounded by either gender differences or cognitive factors, such as educational level.^{13, 15}

The PEA threshold series consisted of 20 concentrations, beginning with a neat solution (0 log vol/vol) and extending in half-log dilution steps to a concentration of -9.5 log vol/vol. Glycerol served as the diluent in this series and as a blank. Stimuli were presented as 18 ml samples in polypropylene squeeze bottles.

Threshold sensitivity was determined via a two-alternative, forced-choice procedure.¹⁶ On each trial, two bottles were presented for subjects to squeeze and sniff, with one containing the diluent and the other a given concentration

of PEA (beginning with -5 log vol/vol). Subjects identified the bottle they believed contained the odor. A single incorrect response led to an increase in concentration on the next trial, whereas two correct responses on consecutive trials caused a decrease. Points where the concentration sequence changed from decreasing to increasing or vice versa were designated "reversals." Five reversals were obtained, and the mean of the log values of the last four served as the measure of olfactory threshold.

Individuals were considered to have suffered a clinically significant loss of smell (i.e., to be hyposmic) if their PEA threshold was greater than -4 log vol/vol. This value represents the upper 2.5th percentile of the distribution of thresholds observed in the present control sample and corresponds exactly to that independently established in a large normative study by the Monell-Jefferson Taste and Smell Clinic.¹⁷

Rhinomanometric assessment

Anterior rhinomanometric evaluation was carried out in 64 patients with AR and 72 control subjects with use of the Rhinotest μ P (I. C. Intertronics, Spring Valley, Calif.). This computerized system provides measurements of right, left, and total nasal airway resistance at 75, 150, and 300 pascal (Pa). Total nasal resistance (TNR) at 150 Pa was used as the measure of nasal obstruction. Because of the considerable variability in nasal resistance in asymptomatic adults, as well as variability in subjective thresholds of discomfort from nasal obstruction, no strict criterion exists for abnormally elevated nasal resistance.¹⁸ For purposes of data presentation and statistical analysis, a relatively conservative value, based on published literature,¹⁹⁻²¹ of TNR greater than 0.35 Pa/cm³/sec was adopted in this study as the criterion for notable nasal obstruction.

Statistical evaluation

Neither olfactory thresholds nor TNR values were normally distributed in the present samples, even after logarithmic transformation. Therefore nonparametric statistical measures (Spearman's rho, the Mann-Whitney U test, and Fisher's Exact Test) were used to assess relationships between nasal patency and olfactory sensitivity, differences between patients and control subjects, and factors discriminating among patients with regard to olfactory acuity.

RESULTS

Questionnaire responses

Fifty-six percent (51/91) of patients with AR reported they suffered from perennial rhinitis, whereas 44% (40/91) reported seasonal symptoms. Of the patients with AR, 35.2% (32/91) indicated they were taking prescription or over-the-counter medication to relieve current nasal and sinus symptoms (antihistamine, decongestant, topical or systemic corticosteroid, and/or antibiotic). More than 80% (75/91) indicated they had some nasal congestion at the time of interview, and 41.8% (38/91) reported this to be moderate or severe.

Among patients with AR, 53.8% (49/91) reported

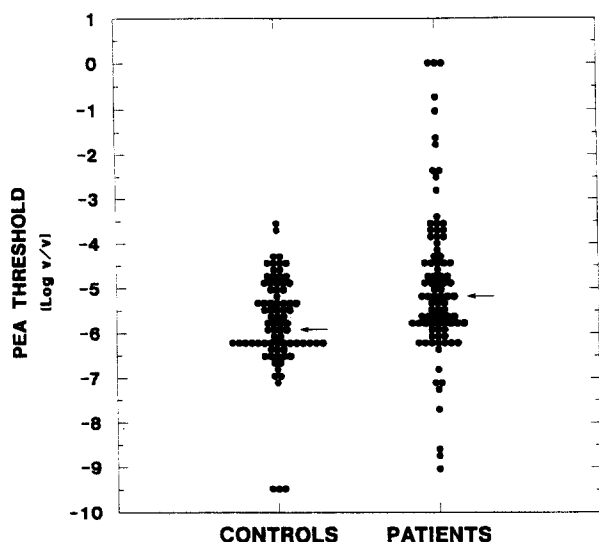


FIG. 1. Olfactory thresholds for PEA in nonatopic control subjects and patients with AR. Median value in each group indicated by an arrow. Threshold concentration expressed as log vol/vol.

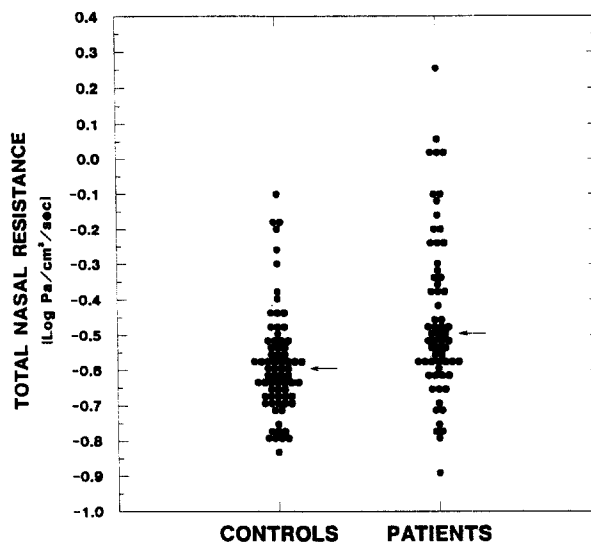


FIG. 2. TNR in nonatopic control subjects and patients with AR. Median value in each group indicated by an arrow. TNR expressed as log Pa/cm³/sec at 150 Pa.

they had experienced a loss or diminution of smell one or more times. This was considered to be a chronic problem by 9.9% (9/91) of the patients, and 17.6% (16/91) indicated they suffered such losses frequently. In 36.3% (33/91) of the patients, sense of smell was thought to be diminished at the time of interview. Patients reporting current nasal congestion were significantly more likely also to report an ongoing loss of smell (Fisher's Exact Test, $p < 0.05$).

Although 33.8% (27/80) of control subjects also reported having experienced a loss or diminution of smell (primarily in relation to head colds), this proportion is significantly lower than that observed among patients with AR (Fisher's Exact Test, $p < .01$). In addition, only one control subject reported smell loss to be a frequent or current problem (this subject believed she had had a gradual, chronic diminution in smell sensitivity with no apparent cause).

Olfactory sensitivity and nasal resistance

As illustrated in Fig. 1, as a group, patients with AR demonstrated significantly higher olfactory thresholds (i.e., lower sensitivity) than control subjects (Mann-Whitney $U = 2473$; $p < 0.001$). In addition, 23.1% (21/91) of patients with AR demonstrated a clinically significant loss of smell, compared with 2.5% (2/80) of control subjects (Fisher's Exact Test, $p < 0.001$). This estimate of the prevalence of hyposmia in AR is somewhat lower but not significantly different from that reported by Seiden et al.⁷ (Fisher's Exact Test, $p > 0.15$).

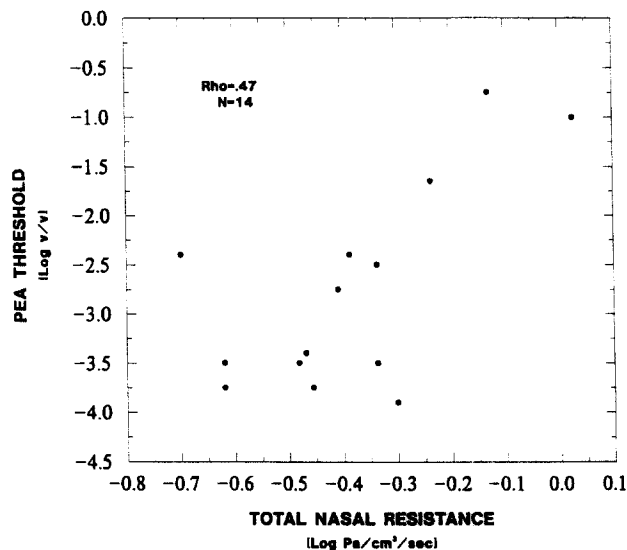


FIG. 3. Scatterplot of relationship between olfactory threshold and TNR in patients with AR who were found to suffer from hyposmia. Threshold concentration expressed as log vol/vol; TNR expressed as log Pa/cm³/sec at 150 Pa.

Nasal resistance was also significantly higher among patients with AR as a group than among controls (Mann-Whitney $U = 1424.5$, $p < 0.001$) (Fig. 2), and significantly more individual patients with AR, 35.9% (23/64), than control subjects, 15.3% (11/72), had markedly elevated TNR (Fisher's Exact Test, $p < 0.01$). There was, however, no overall correlation between TNR and PEA threshold among either patients (Spearman's $\rho = 0.08$) or controls (Spear-

man's $\rho = 0.02$), nor was frank hyposmia in patients associated with pronounced nasal congestion (Fisher's Exact Test, $p > 0.1$). On the other hand, as shown in Fig. 3, if only hyposmic patients are considered, those with greater nasal resistance did suffer from relatively more pronounced olfactory loss (Spearman's $\rho = 0.47$, $p < 0.05$).

Neither the perennial versus seasonal nature of allergy symptoms nor current use of medications to alleviate nasal and sinus symptoms were associated with marked elevations in either olfactory threshold or nasal resistance (Fisher's Exact Test, all $p > 0.1$). There was also no correlation between the number of years patients reported suffering from nasal allergy symptoms and either PEA threshold (Spearman's $\rho = 0.11$) or TNR (Spearman's $\rho = 0.07$).

The presence of secondary nasal and sinus disease in the form of sinusitis or nasal polyps or both (NSD) was, however, significantly associated with diminished olfactory sensitivity (Fisher's Exact Test, $p < 0.006$). Whereas 42.9% (12/28) of the patients with NSD were hyposmic, only 14.3% (9/63) of those with no indications of NSD were. It should be noted, however, that even among the patients with apparently uncomplicated AR, the prevalence of hyposmia was significantly higher than in control subjects (Fisher's Exact Test, $p < 0.02$).

Although the small numbers of patients involved prevent strong conclusions, those with both sinusitis and nasal polyps tended to be more likely to demonstrate significant olfactory loss (5/6: 83.3%) than did those with either sinusitis (6/18: 33.3%) or polyps (1/4: 25%) alone. There was no relation between the presence of NSD and elevated TNR (Fisher's Exact Test, $p > 0.3$).

In six of the hyposmic patients with sinusitis (two of whom also had nasal polyps) repeat assessment of olfactory sensitivity was possible after treatment with an antimicrobial substance. Olfactory thresholds of four of these patients (3 with sinusitis alone; one with sinusitis + polyps) fell within normal limits after treatment.

Finally, patient report of current smell loss was significantly associated with diagnosed hyposmia (Fisher's Exact Test, $p < 0.05$). Report of moderate to severe congestion tended to be associated with marked elevation in assessed TNR, although this relationship fell just short of statistical significance (Fisher's Exact Test, $p < 0.07$).

DISCUSSION

An estimated two million Americans suffer from disorders of smell and taste.²² The results of the present study suggest this estimate is far too low. If our

finding of hyposmia in 23.1% of patients with AR were applied to the 20 to 30 million sufferers of AR in the United States,^{8,9} more than 4.5 million Americans could be expected to have a clinically significant diminution in olfactory sensitivity from this etiologic factor alone. Thus it would appear that AR may be the major single etiologic factor contributing to olfactory disorders.

The prevalence of hyposmia in the present patient sample is not significantly different from that reported in the smaller study of Seiden et al.⁷ Moreover, the percentages of patients reporting a history of smell loss in the two studies are remarkably similar (53.8% and 58.8%, respectively) and extremely high. Of particular note is our finding that more than a quarter of our patients (25/91) considered smell loss to be a frequent or chronic problem for them, compared with only one of 80 nonatopic control subjects.

Patient report of current smell loss was significantly associated with assessed olfactory sensitivity, but these two indexes did not completely correspond. Just as individuals vary in their thresholds for discomfort from nasal obstruction,¹⁸ they appear to vary in their awareness of changes in olfactory sensitivity. Given the variability in olfactory sensitivity observed among control subjects, we cannot rule out the possibility that patients who reported diminished smell but whose thresholds fell within the normal range had had a relative loss in sensitivity.

Others have reported the absence of a relationship between measures of nasal airflow resistance and olfactory sensitivity in healthy subjects.^{23,24} We also failed to observe a significant relationship between nasal patency and olfactory sensitivity in healthy control subjects. In addition, we found no relationship between these two measures across our patient sample, despite the extremes in both TNR and olfactory thresholds observed in patients with AR. The conditions under which olfactory function is tested, in which subjects make a conscious effort to inhale directed odor stimuli, may partially obscure the impact of nasal congestion on the ability to perceive odors in the natural environment. Nonetheless, it appears that even substantial obstruction of the lower nasal airway is not sufficient to produce a clinically significant reduction in olfactory sensitivity. It is of interest, however, that separate consideration of hyposmic patients only revealed a significant, positive correlation between TNR and olfactory threshold. That is, given the conditions that give rise to hyposmia in AR, restrictions in total nasal airflow may exacerbate the problem.

Our results suggest that sinusitis and nasal polyps are key factors in allergy-related hyposmia. This is

consistent with the findings of Fein et al.,¹ based on patient report of smell loss, and as in that study, there is a suggestion that the combination of sinusitis and nasal polyps is most likely to result in hyposmia. Even among patients with AR who were apparently free of NSD, however, the prevalence of hyposmia was significantly higher than that observed in control subjects.

Other investigators have reported that allergy-related hyposmia often responds to corticosteroid therapy,^{1, 4, 25} whereas we observed return to normal olfactory function in several hyposmic patients with sinusitis after antimicrobial therapy. These observations suggest that inflammatory conditions of infectious or allergic origin may produce reversible hyposmia through local obstruction of the olfactory epithelium or other factors directly related to the inflammatory process. Thus the type of smell dysfunction observed in many patients with AR is also likely to occur in nonallergic patients with NSD. At the same time, however, the present results leave open the possibility that other factors specific to the allergic process may play a role in allergy-related hyposmia.

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