

Allergy practice and the otolaryngologist

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Allergic conditions in the upper airways, particularly in the nose, are common and should be considered in all patients who visit an otolaryngologist. The increasing number of patients with allergic disorders, as well as the multifactorial etiology, creates a need for both medical and otolaryngic allergists. The otolaryngologist treats many disorders in the nose, not only those requiring surgical treatment but also those that require immunologic management using standardized extracts for skin testing, radioallergosorbent tests, and immunotherapy. The otolaryngologist should be familiar with recent knowledge about T lymphocytes, inflammatory biomarkers, *ie*, cytokines and adhesion molecules, and neuropeptides in sensory nerves. Awareness of the most up-to-date progress in information technology related to the decision-making process is also helpful. By these means the otolaryngologist should be able to master the management of allergic and nonallergic disorders of the nose.

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Both medical allergists and otolaryngic allergists offer care to patients with allergy in the upper airways. Is it rational for both specialties to care for the same patient population? The medical allergists want to protect themselves, because they perceive a reduction in resources as a threat to their discipline [1•]. However, a struggle between allergists and otolaryngologists is a no-win situation; both disciplines are needed to treat the ever-increasing number of allergic patients. The otolaryngic allergists should join the medical allergists in the complex management of allergy problems [2••]. A patient with nose problems might be regarded primarily as having an infection when seen by a general practitioner, an anatomic deviation by an otolaryngologist, an immunologic disorder by an allergist, and anxiety by a psychiatrist. All and none are correct! The multifactorial etiology and multiple manifestations of allergy warrant a close collaboration not only with allergists but also with general practitioners, pediatricians, pneumologists, and dermatologists [3]. However, otolaryngologists have the advantage of being problem-oriented organ specialists, whereas medical allergists are mechanistically oriented. In the patient with nasal complaints, the otolaryngologist will consider causes other than allergy.

This review discusses how the otolaryngologist can confidently treat patients with allergy in the upper air-

ways, particularly allergic rhinitis, by keeping current with aspects of etiology, pathophysiology, diagnosis, and treatment. Perhaps the otolaryngic allergist should behave as a "rhinologist." In Europe, the ear, nose, and throat discipline is referred to as *otorhinolaryngology*, a term that emphasizes the importance of the nose.

Increasing frequency of allergy and role of environment

The prevalence of symptoms of allergic rhinitis is increasing in many countries [4], *eg*, in Sweden, 4.4% in 1971, 8.4% in 1981, and 18% in 1991 [5,6]. The reason for this increase is far from clear. Although many patients are born atopic [7], becoming allergic from environmental exposure should not be inevitable. Exposure to a changing environment—indoor as well as outdoor air pollution—has been suggested as one important reason for the increase of patients with allergic rhinitis [8••]. Occupational rhinitis can now be confirmed by immunologic tests [9]. The role of the environment has been questioned, however, because in Poland, which is known to be a rather polluted country, the prevalence of allergy is lower than in less-polluted countries [10]. On the other hand, smoking is known to contribute to allergy [4], *eg*, children born to

Abbreviations

CGRP—calcitonin gene-related peptide; RAST—radioallergosorbent test; SP—substance P; SPT—skin prick test.

smoking mothers have more allergies than those with nonsmoking mothers. Nasal manifestations of allergy to food, including preservatives and additives, occur rarely as a single symptom, as confirmed in 0% to 35% of those patients who had positive skin and in vitro test results before being challenged with food in a double-blind, placebo-controlled fashion [11].

Mechanisms of allergy

Inflammatory markers in the nose

To better discriminate patients with nasal allergy from those without allergy, we need to know about the type of ongoing inflammation [12]. The otolaryngologist not only should learn more about inflammatory mechanisms but also should use his manual skills to sample tissues by means of lavage fluid, brushing, scrapings, and biopsies from the nose. The degree of inflammation is reflected by the concentration of biomarkers determined from nasal lavages [13,14]. Albumin is an inflammatory biomarker of plasma leakage. It is found to increase in allergy, but it cannot be used to discriminate allergic from nonallergic rhinitis because albumin also increases in conditions such as infectious rhinitis [15]. The type of inflammation can also be determined by measuring inflammatory cells, *eg*, neutrophils, eosinophils, monocytes and macrophages, and mast cells in nasal lavage fluid [16•]. Then, not only the number but also the activity of the inflammatory cells should be determined. Determining the so-called EG2-antibody on eosinophils in the nose helps to differentiate allergic patients from nonallergic patients [17]. The recent knowledge about the communication between inflammatory cells by means of adhesion molecules [18•], cytokines [19], and chemokines [20•], of which the so-called RANTES seems to be one of the most exciting [21], provides us with promising tools for discrimination of different nasal disorders.

Nerves

Increasing evidence indicates that neuropeptide-containing sensory nerves have an important role in allergic rhinitis [22]. Neuropeptides, such as substance P (SP) and calcitonin gene-related peptide (CGRP), increase in nasal lavage fluid after antigen challenge [23]. SP and CGRP affect the upper airways [24], but the effects are weak, probably because of enzymatic degradation by peptidases, such as neutral endopeptidase [25], which increases in nasal lavage fluid after antigen challenge [26]. Topical application of capsaicin, the pungent principle of hot red pepper, depletes SP and CGRP from the nasal mucosa [27]. Treatment with capsaicin has been successful in patients with nonallergic rhinitis [28,29] but has not been tried for treatment of allergic conditions.

Allergy as part of a systemic disease

Medical allergists often claim that they should treat patients with allergic rhinitis because it is part of a systemic disease, which in fact, is true. This connection with systemic disease has been demonstrated by skin prick test (SPT) and radioallergen sorbent test (RAST) and provides the rationale for immunotherapy. Furthermore, patients with allergic rhinitis have a greater risk of developing asthma than those without allergic rhinitis [30]. Similarly, treatment of allergic rhinitis with local corticosteroids improves asthmatic symptoms [31]. The otolaryngologist must be able to evaluate the lower airway function, too. However, patients who require daily intake of bronchodilators should be referred to a medical allergist or pneumologist.

Allergy and allergy-like conditions

Differential diagnoses

In otolaryngologic practice, not all patients with nasal complaints suffer from allergy; in fact, probably fewer than one half of the patients are allergic [32]. The real challenge for an otolaryngologist is considering alternate diagnoses for those patients who prove not to be allergic. Seasonal rhinitis is not a diagnostic problem, but perennial rhinitis is. In perennial rhinitis, determination of inflammatory cells and biomarkers might be helpful [33,34•,35,36•].

A crucial question in chronic nasal complaints is whether a test-confirmed allergy occurs as a single or as a coincidental cause to the patient's problem, because allergy is common. The nonotolaryngologist and the otolaryngologist, of course, should be alert for unilateral complaints, such as bleeding and aching, and should always regard such symptoms seriously. The allergist should refer the patient to an otolaryngologist. A history of rhinitis not only might mask a coincidental occurrence of cancer but also might imply a higher risk of developing cancer, probably because of exposure to the same risk factors existing in the environment [37]. Other differential causes of nasal complaints, single or coincidental, which are best evaluated by the otolaryngologist, include septum deviation, alar insufficiency, nasal polyps, adenoids, papilloma, infection, and hypertrophied turbinates due to abuse of decongestants, *ie*, rhinitis medicamentosa. Allergic patients are more infected, and patients with chronic rhinosinusitis should be tested for allergies because an allergy might be masked, *eg*, mite allergy [38].

Nasal polyps

Nasal polyps are not caused by allergic conditions and are no more frequent in allergic patients than in nonallergic patients [39–41]. Although eosinophils are present in polyps, there seem to be ways other than through a typical IgE-mediated hypersensitivity by which eosinophils can be recruited [42,43]. Otolaryngologists should keep up with current immunologic

knowledge regarding new possibilities in the treatment of polyps.

Rhinoscopy and endoscopy

Patients with chronic nasal complaints should be examined by nasal inspection by means of rhinoscopy and endoscopy before and after decongestion to evaluate the degree and localization of the disease [44]. Medical allergists, as well as otolaryngic allergists, are trained in the use of fiberoptic rhinoscopy [45].

Allergy manifestations at ear, nose, and throat clinics

Allergy affects not only the nose but also the ears, mouth, throat, and larynx. It is essential, therefore, that the otolaryngologist consider the possibility of allergy in most patients who visit an ear, nose, and throat clinic. Middle ear diseases are sometimes found to be more common in atopic than nonatopic children [46]. On the contrary, children with adenotonsillar disease are not associated with a higher prevalence of allergy [47]. When a patient presents with edema of the mouth and throat, allergy might be easy to suspect if the patient refers to the intake of some unusual food. The same symptoms may be more difficult to evaluate, however, if related to the inhalation of enzymes used in the biotechnology industry [48]. The otolaryngologist must also be aware of allergy in the operating room, especially during the administration of anesthesia [49] and when using latex gloves [50].

Clinical history, skin tests, and in vitro tests

To confirm allergy when suspected and to exclude allergy when not suspected, we need reliable tests. First, a precise clinical history is required. Although, clinical history is sufficient in most cases of seasonal allergy, confirmation by SPT or RAST, or both, might be necessary in multiple allergies and when diagnosis is not obvious, *eg*, perennial allergic rhinitis. Some years ago, most allergists used endpoint titration by the intradermal test method. That method has been more or less abandoned, at least in Europe, because of the lack of reproducible results [51]. However, skin endpoint titration still seems to be used in the United States [3]. In Europe, only one concentration of the allergen extract is used for the SPT with a resulting high degree of both specificity and sensitivity [52,53]. For screening in perennial rhinitis, it might be helpful to use Phadiatop microscreen (Pharmacia Diagnostics, Piscataway, NJ), which expresses the highest level of one of several antigens when the results are positive but does not express the individual results [53]. Phadiatop should be followed by SPT or RAST, or both, to get a specific diagnosis. SPT or RAST provide equal information, but

SPT yields a faster result and is cheaper than RAST. However, in patients affected with eczema, RAST might be preferred. In patients considered for immunotherapy or for specific elimination, the suspected diagnosis should be confirmed by a nasal provocation test [52–54]. However, the evaluation of the clinical history, SPT, and RAST has to be done carefully. This evaluation differs among antigens, patients, laboratories, and offices. Therefore, the extract used for SPT and RAST should be standardized in order to compare different antigens and to avoid false-positive and false-negative results.

Treatment

Treatment of allergic rhinitis is based on the strategies to prevent the release of mediators, to prevent the effect of the mediators released, and to desensitize the patient. Prevention and elimination of the antigen should be tried first. Knowledge of aerobiology and environmental pollutants is necessary for the otolaryngologist in order to give the patient proper advice.

Pharmaceuticals

Local corticosteroid treatment is regarded as the first-choice treatment in patients with allergic rhinitis, resulting in a total control of symptoms in 40% [55•,56]. Treatment with nonsedative antihistamines alone or in combination with local corticosteroids is a good alternative. Although frequently used, topically applied corticosteroids cause few side effects. When side effects occur, however, the patient needs to see an otolaryngologist. A rhinologist is used to treating symptoms such as septum perforation, bleeding, and atrophy with dryness [57•]. Likewise, the rhinologist may be confronted with patients who abuse topical decongestants, *ie*, those presenting with rhinitis medicamentosa, and may need to treat side effects resulting from misuse of both topical and oral vasoconstrictors [58].

Immunotherapy

Immunotherapy is an alternative to patients who do not respond adequately to antiallergic drugs [59]. Immunotherapy is regarded as effective and safe; systemic effects are rare but might occur in patients with asthma and in those who are sensitive to mites [60,61,62•], always within 30 minutes [63]. The classical immunotherapy involves induction of T-cell intolerance [64•,65•] and is now evolving to a peptide therapy [66], which may allow more precise doses and fewer side effects. Alternate routes, such as the nose and mouth, have also been tried and have been proved effective [67,68]. They are not widely used, however, because of the costs, at least for the oral immunotherapy. Otolaryngologists should be trained to perform immunotherapy; they already treat alarming systemic effects, such as airway edema with obstruction.

Allergy and surgery

Whereas medical allergists might underestimate the role of anatomy in nasal complaints, the otolaryngologist might overestimate it. Allergy might be the major cause of the patient's problem, rather than a narrow ostio-meatal complex. However, it seems that the effect of immunotherapy on patients does not change the middle meatotomy patency [69]. In addition, a substantial number of patients who undergo immunotherapy stop after functional endoscopic sinus surgery because their symptoms resolve or are minimized [70]. Conceivably, the otolaryngologist should be prepared for both a surgical and a medical approach, because the patient might suffer from allergy as well as a septal deviation concomitantly. Furthermore, surgery of the nose might facilitate the administration of local therapy.

Quality assurance and information technology

To validate the treatment of the allergic patient and compare with others, symptoms, signs, treatments, and results should be documented in a systematic fashion. A computerized questionnaire might be helpful [71]. With complicated clinical histories, an increasing number of tests, and biomarkers, computers will facilitate the use of databases as a resource for medical decision making and quality assurance tests [72,73]. The otolaryngologist should use the information technology in his or her allergy practice.

Conclusions

The otolaryngic allergist should regard himself or herself as a rhinologist who knows much about the upper airway and takes care of both allergic and nonallergic conditions of the nose. The otolaryngologist should be trained for and master all aspects of the diagnostic procedure of suspected allergy including a careful clinical history, SPT, RAST, provocation test, evaluation of biomarkers in nasal fluid, rhinoscopy, endoscopy, and imaging. The treatment of allergy involving elimination and the role of the environment, pharmaceuticals, immunotherapy, and surgery should also be familiar to the otolaryngologist. Personal interest and skills and local organizations have to decide which specialist should help the patient with nasal complaints. Rigid departmentalization of work is not in the best interest of the patient. Increased experience and knowledge in allergy and immunology [74], however, will assist the otolaryngologist in treating allergic and nonallergic patients.

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