Vocal allergy: recent advances in understanding the role of allergy in dysphonia

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Purpose of review

To examine recent advances in our understanding of the laryngeal effects of allergies with particular attention to the impact on vocal production.

Recent findings

A growing body of literature suggests an association between allergies and dysphonia evidenced by the increased likelihood of singers with vocal complaints to self-identify allergic rhinitis by standardized questionnaire compared with singers without vocal complaints, the severity of vocal symptoms of allergic patients in relationship to nonallergic controls, and the increased vocal complaints of allergic individuals from the nonallergy to allergy seasons. Arguments have also been made for the misdiagnosis of allergic dysphonia as laryngopharyngeal reflux disease. A recent study has demonstrated the first evidence of a causal relationship between allergen exposure and voice changes in the absence of a sinus or lower airway allergic response.

Summary

New evidence has highlighted the likelihood that allergies are indeed associated with dysphonia. The existence of a direct allergic response in the larynx has meaningful implications for the diagnosis and treatment of dysphonia. Further research is needed to identify the underlying pathways mediating the laryngeal response to allergy so that improved diagnostic and therapeutic techniques can be developed.

Keywords

allergic laryngitis, dysphonia, laryngeal allergy, laryngopharyngeal reflux disease

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Introduction

Laryngeal allergy is a topic that has received little attention in the literature. The very existence of laryngeal allergy has been questioned [1] but recent evidence is beginning to highlight the role of allergy in dysphonia [2••,3•,4••]. The purpose of this review is to highlight recent advances in our understanding of the laryngeal effects of allergies with particular attention to the impact on vocal production. The clinical and therapeutic implications with respect to differential diagnosis, ramifications for current treatment models, factors that should be considered in the therapeutic interventions of individuals with allergy-related vocal complaints and directions for future research will be discussed. The most recent comprehensive review on the effect of allergies on voice was published over 7 years ago in 2003 [5]. Since a limited number of yearly publications on laryngeal allergy have been published, we review key studies since that time including a comprehensive review of the literature over the last 2 years. Additional information can be found in two reviews by Chadwick [5,6].

Background

The negative impact of allergies on vocal function is a notion that goes unquestioned by singers, actors, clergy, broadcasters and other professional voice users with allergies. For these individuals who complain of changes in both vocal quality and function during allergic episodes, the anecdotal link between allergies and voice is obvious. Even subtle changes to the mucosal cover of the vocal folds or secretions of the larynx can pose a significant handicap for a singer [1,7,8]. There has also been anecdotal evidence reported in the medical literature indicating a probable link between allergies and vocal dysfunction for at least 40 years [1,9]. This association has been observed with food allergy [10–13], inhalant allergy [14–16] and sensitivities to chemicals and organic substances [17,18]. Despite consistent anecdotal evidence indicating allergy as a possible cause of vocal dysfunction, there is a paucity of data in the literature regarding the direct effects of allergy on the larynx and no clear causal model has been described establishing allergy as a cause of vocal dysfunction. The studies of allergy-related vocal

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dysfunction that do exist are mostly case studies, retrospective research, uncontrolled prospective clinical designs and survey research. Although attempts have been made to investigate the laryngeal effects of allergy in a controlled fashion [2••,19], these attempts have been hampered by pulmonary complications necessitating the termination of further attempts.

Given the lack of controlled studies regarding the contributions of allergy to dysphonia, especially within the context of highly suggestive anecdotal evidence, a better understanding of the relationship has important clinical and research implications. Although the exact frequency of allergy-related dysphonia is currently unknown, Williams [12] attributed allergy as the primary cause of dysphonia in 28% of his patients once all other possible causes were ruled out. If his experience is even partially representative, then, as a number of authors have suggested, allergy-related dysphonia is most likely being misdiagnosed or underdiagnosed [3•,10]. Misdiagnosis of allergy-related dysphonia has meaningful health consequences considering girls with allergies are at long-term risk of dysphonia [20], individuals with occupational laryngitis and unresolved laryngeal symptoms are more likely to develop asthma than individuals with resolved laryngeal symptoms [21], and people with allergies are more likely to have voice problems [22].

Controversy I: processes underlying laryngeal symptoms of allergy

From a theoretical as well as clinical viewpoint allergic laryngitis is not currently considered an independent disease process but rather a secondary sequela to another disease process such as allergic rhinitis or asthma [5,23]. The underlying process leading to vocal complaints has been suggested to be mediated by postnasal drip from the sinuses, which leads to local irritation, throat clearing and resultant dysphonia [5], or a result of an impairment in nasal breathing and altered resonance characteristics of the upper airway [1]. The current clinical approach to remediating laryngeal symptoms is to treat the underlying allergic rhinitis or asthma. However, there have been studies of individuals with vocal complaints in the absence of upper airway symptoms [10], or of those who have persistent vocal complaints following treatment of allergic rhinitis with nasal steroids that subsequently resolve with immunotherapy [24]. The lack of improvement in vocal complaints despite treatment of the sinus symptoms calls into question the requisite role of the sinuses in mediating a laryngeal response. Additionally, the successful resolution of the vocal complaints and asthmatic symptoms after immunotherapy suggests that the vocal symptoms may be the result of a localized allergic response in the larynx or systemic allergic pathway acting on the airway as a whole. The latter view is one held by Morice [25], who indicated that any decrease in lower airway symptoms as a result of intranasal inhaled steroids is likely the result of a generalized decrease in airway inflammation rather than a reduction in postnasal drip.

Additional questions regarding a role for postnasal drip in the allergic response of the larynx comes from studies using radiographic tracing of upper airway secretions. Although radiographic evidence has shown aspiration of nasal secretions in a group of cognitively compromised patients with decreased consciousness and slightly less than half of normal individuals during sleep [26], a recent study of individuals with sinusitis and asthma showed no evidence for aspiration of nasal secretions over a 24 h period [27]. The authors suggest that the coexistence of upper and lower airway disease is the result of a generalized response of the continuous mucosal lining of the upper and lower airways. Collectively, these results challenge the likelihood that the aspiration of sinus secretions serves as an intermediary between an initial allergic response in the upper airway which is then propagated to the larynx and lower airway via postnasal drip. A more likely explanation for the concomitant presence of sinus and laryngeal symptoms is that a generalized process underlies inflammation along the continuous mucosal lining of the upper and lower airway. Around 20 years ago, this concept was codified as the unified airway which links upper and lower airway inflammation [28–30]. This new understanding recognizes that the airway functions as a single organ system including the larynx and that inflammation initiating in one part of the system can propagate throughout the respiratory tract via local and systemic processes.

Evidence for laryngeal allergy: historic challenges

The paucity in the literature of evidence for, or even investigations into, the direct response of the larynx to allergy is related to a number of practical and technological factors. Until very recently, no paradigm has existed for safely studying the laryngeal allergic response independent of responses in the sinuses and lower airway. Without a means to control for these factors any measured changes in vocal function or appearance could not be attributed to a primary process operating at the laryngeal level. The presence of an allergic response in the sinuses would obfuscate whether the origin of any measured changes in vocal function was the result of some type of inflammatory process within the larynx, laryngeal irritation produced by secretions migrating from the sinuses or a generalized airway response initiated by the sinuses. Similarly, in the presence of any simultaneous lower airway inflammation or constriction, which

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can independently alter vocal production [31,32], there would be no way to know whether measured changes in vocal function were related to laryngeal inflammation or restricted airflow from the concomitant lower airway response.

Relationship between allergies and dysphonia

Although empirical support in the literature for the existence of allergic laryngitis is almost nonexistent, a slowly growing body of literature suggests an association between allergies and dysphonia, converging on the likelihood that allergies can play a significant role in the development of dysphonia. A retrospective review comparing singers with vocal complaints but no neurological or anatomical cause with singers without vocal complaints found that the singers with vocal complaints were 15% more likely to be identified by a standardized questionnaire as having allergic rhinitis [33]. This likelihood rose to 25% for singers with two or more vocal symptoms. In total, 93% of the singers with vocal complaints were identified as having allergic rhinitis. Simberg and colleagues [15] investigated the frequency of specific vocal complaints in patients with allergies compared with nonallergic controls. The individuals with allergies had significantly more severe voice symptoms than nonallergic controls. Thirty-nine percent of individuals with allergies had two or more vocal symptoms. There was no significant difference between allergic individuals with or without asthma so these vocal complaints could not be attributed to asthma. In contrast, only 11% of patients without allergies reported two or more vocal complaints.

Millqvist and colleagues [34•] followed a group of allergic patients and nonallergic controls through the birch pollen and nonpollen seasons using a self-rated vocal symptom score along a visual analog scale (VAS) and Voice Handicap Index (VHI) scores. The VHI [35] is a validated measure of the negative impact of vocal problems on quality of life and one of the most frequently used tools for measuring research and clinical outcomes. The allergic individuals reported a significantly greater increase in VAS-rated vocal symptoms from the nonpollen to pollen season than did nonallergic individuals. Additionally, the VHI scores for patients with allergies were significantly higher during pollen season than the scores for controls without allergies. The negative impact of allergies on voice-related quality of life was also seen in a recent study by Krouse and colleagues [36]. A consecutive series of 47 adults without current allergic or vocal complaints were tested for sensitivity to dust mite by skin prick testing and divided into two groups based on a positive ($n = 21$) or negative ($n = 26$) response. Although no differences between the groups could be found based on a number of aerodynamic and acoustic measures, auditory and visual perceptual ratings by expert judges or various parameters on larnyngovideostroboscopic evaluation, the two groups were significantly different from one another on total VHI scores. This suggests that self-perceived vocal handicap is greater in allergic individuals than in individuals without allergies even in the absence of current symptoms and that the impact of allergies on voice may appear before these changes can be identified with current clinical tools. Further support for individuals' identification of vocal symptoms in the absence of clinical detection comes from an organic dust provocation study in which patients' self-ratings of vocal symptoms along a VAS significantly increased postchallenge despite the lack of a significant difference in the clinicians' ratings of vocal quality [37]. These recent studies along with earlier studies in the literature [10–14,16,17,20, 22,38] are highly suggestive of a relationship between allergies and vocal dysfunction but are by no means proof for the existence of allergic laryngitis.

Emerging evidence of allergic laryngitis

Although a number of studies have been able to suggest some type of an association between allergies and dysphonia, until recently no study has documented a definitive causal relationship between allergen exposure and a direct allergic response in the larynx causing dysphonia. As mentioned earlier, in order to prevent any laryngeal changes from allergen provocation testing from being attributed to a secondary response from the sinuses, it is necessary to prevent any antigen from entering the nares. Although peroral provocation methods have been used previously by spraying antigen onto the soft palate or pharynx to obviate the sinuses [18,39], it was Reidy *et al.* [19] who developed the first transoral provocation method using nebulized antigen, thus allowing the antigen to directly enter the larynx. The outcome measures used in this first study were unable to capture any significant changes in laryngeal function with the concentration of dust mite administered but a general trend in the data indicated a possible effect on vocal function. To investigate this possibility further, the authors undertook a second study using a higher concentration of nebulized antigen [2••]. This second study highlights the significant challenges posed by direct laryngeal provocation testing as the first two patients suffered significant pulmonary reactions necessitating a termination of the study. In addition to the respiratory reactions, both of these patients also demonstrated vocal fold edema and erythema, an increase in endolaryngeal secretions, mild coughing, and hoarseness. However, the source of increased secretions could not be definitively attributed to the larynx in the presence of coughing and bronchospasm which could have transported the mucus from the lower airway. Additionally, any perceived changes in

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vocal quality could have been a result of coughing rather than an allergic inflammatory response of the laryngeal mucosa.

In order to control for any pulmonary reactions in addition to bypassing the sinuses, Roth *et al.* [4••] employed the transoral provocation method described by Krouse and colleagues [2••,19] but excluded all individuals who demonstrated a reactive airway on methacholine challenge testing. In addition, individualized antigen concentrations were determined for each patient by gradually increasing antigen concentration levels while measuring for an increase in the subglottic pressure required to initiate phonation (which is indicative of a change in tissue and secretion viscosity) and monitoring airway patency after each challenge with pulmonary function testing. The established antigen concentration for each individual was used during a subsequent double-blinded, placebo-controlled, provocation challenge study during which the effect of antigen challenge on subglottic pressure was compared with the effect from saline placebo. These additional safety precautions helped prevent coughing, wheezing or other pulmonary reactions. All five patients had a significant increase in the subglottic pressure required to initiate phonation of between 1.85 and 4.87 standard deviations above their respective baseline means. This is the first study to indicate a causative relationship between allergy and vocal function independent from any sinus or pulmonary signs or symptoms [4••].

Controversy II: vocal allergy vs. laryngopharyngeal reflux disease

Despite its near universal acceptance among laryngologists, the diagnosis of laryngopharyngeal reflux disease (LPR) is still controversial [40]. The similarity in the reported signs and symptoms of vocal allergy with LPR complicates the differential diagnosis between dysphonia related to allergies and LPR. A comparison of the laryngeal symptoms attributed to allergy and LPR can be found in Table 1 and the laryngeal signs attributed to each can be found in Table 2. The four most commonly reported signs and symptoms are shared between LPR and vocal allergy. The nonspecific nature of these signs and symptoms is problematic diagnostically and has led to debate regarding their sensitivity and specificity [41] and ultimately their utility as diagnostic criteria. The implication is that symptoms suggesting LPR could have a number of underlying causes including allergy, which has led some authors to suspect that LPR is currently over-diagnosed [42•]. The variable benefits of proton pump inhibitors to resolve vocal complaints attributed to LPR are often cited as a possible indication that the cause of these nonspecific laryngeal symptoms may be related to another cause such as allergy [40,42•]. Randhawa *et al.* [3•] investigated 15 consecutive patients diagnosed with a primary voice disorder (no anatomical or neurological cause) for the presence of LPR using the reflux symptoms index (RSI) and reflux finding score (RFS) and for the presence of allergy using skin prick tests and nitric oxide. A total of five patients were negative for both LPR and allergies, whereas the remaining 10 patients tested positive for allergies. Of those 10 patients, three were also positively identified as having LPR, raising questions regarding the specificity of the reflux tests. The fact that three times as many patients were identified as having allergies than LPR suggests the possible overdiagnosis of LPR.

Table 1 Comparison of symptoms attributed to dysphonia from allergy and laryngopharyngeal reflux disease (LPR)

Symptom	Allergy	LPR
Throat clearing	X	X
Chronic cough	X	X
Globus	X	X
Hoarseness, voice change	X	X
Excessive mucus	X	X
Postnasal drip	X	X
Sore throat, throat discomfort	X	X
Itchy eyes	X	
Nasal congestion	X	
Dysphagia, problems swallowing		X
Heartburn		X

The most commonly described symptoms are in bold. The symptoms presented represent a composite of those frequently described in the literature [10,14,16,23,33,36,40,41,42•,43–47].

Therapeutic implications for the diagnosis and treatment of dysphonia

The most common diagnoses assigned to individuals with nonorganic dysphonia have been LPR or muscle tension dysphonia. An allergic cause has often only been considered if proton pump inhibitors and voice therapy have failed to ameliorate the symptoms. Given the lack of conclusive evidence surrounding the existence of laryngeal allergy and the abundance of research activity supporting a role for LPR in the manifestation of dysphonia this has been an expedient approach. However,

Table 2 Comparison of clinical signs attributed to dysphonia from allergy and laryngopharyngeal reflux disease (LPR)

Sign	Allergy	LPR
Diffuse laryngeal edema	X	X
Vocal fold edema	X	X
Excessive mucus	X	X
Thick viscous mucus	X	X
Vocal fold erythema	X	X
Arytenoid erythema	X	X
Hypertrophy of posterior larynx		X
Granuloma formation		X

The most commonly described signs are in bold. The signs presented represent a composite of those frequently described in the literature [10,14,16,23,33,36,40,41,42•,43–47].

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considering recent suggestions that LPR is being overdiagnosed, the growing body of literature indicating a relationship between allergy and dysphonia and a preliminary study demonstrating causality between allergen provocation and dysphonia, allergy should be considered as a possible source of nonorganic dysphonia earlier in the diagnostic process.

The treatment approach for allergy-related dysphonia requires further study. The current pathway is to first treat the sinus symptoms with nasal steroids and avoid the use of antihistamines if possible because of their potential drying effect on the laryngeal mucosa. For professional voice users this has included avoiding even the most recent generation of antihistamines. Although there is some indication that localized treatment of sinus symptoms may have a generalized effect of reducing inflammation throughout the airway, more information is necessary to determine whether systemic treatments such as immunotherapy may better control any localized reactions in the larynx. The cost–benefit ratio of treatment with antihistamines should also be evaluated to determine whether their therapeutic benefit outweighs any potential drying effect on the larynx.

Conclusion

The relationship between allergies and vocal dysfunction has received little attention in the literature in part because of practical and technological limitations in studying the phenomenon. A recent study demonstrated a well tolerated and practical method of oral inhaled allergy provocation that bypasses the nose and limits the potential for a pulmonary response by excluding patients with asthma and a positive methacholine challenge. Preliminary results have shown that allergy challenge can cause dysphonia. Further investigations into the underlying inflammatory mechanisms mediating the laryngeal response to allergy are necessary to advance current diagnostic and treatment methods. Once we are better able to understand and identify the processes involved in the laryngeal allergic response we will be in a better position to differentiate dysphonia related to allergy from that caused by LPR or other forms of dysphonia currently lacking specific findings. We will also be able to develop new treatment regimens based on knowledge of the underlying processes, allowing less trial and error in the treatment of patients' nonorganic dysphonia.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

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Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

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