Controversies and Confusions in Diagnosing Laryngopharyngeal Reflux

Robert Sataloff

The problem of reflux has become well known among singing teachers. It is recognized as common for reasons that have been discussed extensively in previous literature. While being careful not to get too confused, it is worthwhile for singing teachers to recognize that diagnosis and treatment of reflux in singers and other otolaryngology patients remain more controversial than we would like.

Laryngopharyngeal reflux (LPR) is an extraesophageal variant of gastroesophageal reflux disease (GERD) that affects the larynx and pharynx. In recent years, many otolaryngologists have acknowledged the existence and potential importance of LPR in patients with otolaryngologic complaints, although the association between acid reflux and laryngeal abnormalities has been recognized for more than four decades. As otolaryngologists have been more diligent about looking for signs of LPR such as posterior laryngeal edema (swelling) and erythema (redness), obliteration of the laryngeal ventricles and interarytenoid hypertrophy, treatment for LPR based upon these findings has become increasingly common. Because of a paucity of convincing evidence regarding techniques for establishing definitive diagnosis and causation in individual patients, and because of a plethora of imperfect studies that have produced conflicting conclusions, LPR diagnosis and management remain controversial. Nevertheless, most recent evidence suggests that LPR represents a complex spectrum of abnormalities. It is essential for otolaryngologists and gastroenterologists (as well as other healthcare providers) to understand the latest concepts in basic science and clinical care of patients with LPR.

Symptoms and signs of LPR have been reported in 4% to 10% of all patients seen by otolaryngologists, but it is likely that these estimates are low. Among patients who present with voice disorders, the estimated prevalence is much higher. In 1989, Weiner et al. reported that 78% of 32 patients with voice complaints had LPR documented by pH probe. Koufman et al. found LPR in 78% of patients with hoarseness, and in roughly 50% of all patients who presented with voice complaints. Many other publications have addressed the pathogenesis of voice disorders and otolaryngologic manifestations of LPR, as well as its prevalence. Yet, definitive epidemiological studies to confirm the prevalence and otolaryngologic consequences of LPR are still lacking. Consequently, while many physicians believe the condition is still underdiagnosed, many also suspect overdiagnosis and misdiagnosis in many patients.
LPR is believed to damage the larynx either directly, or secondarily. Direct injury is due to the contact of acid and pepsin with laryngeal mucosa, resulting in mucosal injury.\(^8\) Alternatively, laryngeal irritation and injury may be produced without direct acid contact with the larynx when irritation of the distal esophagus by acid triggers a vagus nerve response that produces chronic cough and throat clearing capable of traumatizing laryngeal mucosa.\(^9\) Bile reflux also may be a cause of laryngeal mucosal inflammation.\(^10\)

Other, more sophisticated, factors may be important, as well. For example, Eckley reported that decreased salivary epidermal growth factor appears to be associated with LPR;\(^11\) and Altman discovered a proton pump in laryngeal serous cells and ducts, raising additional intriguing questions about the pathophysiology of LPR.\(^12\) It has been long asserted that non-acid reflux also can trigger cough and throat clearing and cause mucosal irritation that is troublesome to some voice patients, and recent experience with impedance monitoring has confirmed the association between non-acid reflux and such symptoms.

LPR has been associated with numerous laryngeal conditions including muscle tension dysphonia, Reinke's edema, globus sensation, laryngeal hyperirritability, laryngospasm, delayed wound healing, posterior laryngitis, diffuse laryngitis, laryngeal pyogenic granuloma, glottic and subglottic stenosis, cricoarytenoid joint ankylosis, carcinoma and other conditions.\(^13\) It also has been associated with sudden infant death syndrome,\(^14\) probably mediated through the laryngeal chemoreflex.\(^15\)

Traditionally, otolaryngologists have managed patients with LPR by therapeutic trial. If definite improvement in symptoms and signs is noted after treatment with a proton pump inhibitor (PPI), some physicians consider the diagnosis confirmed. For patients who show no response to reflux therapy, some otolaryngologists assume reflux has been ruled out and discontinue the PPI, substituting treatment for allergy or some other condition. In the absence of studies, this approach is particularly problematic since many patients continue to produce at least some acid despite proton pump inhibitors twice daily, and it has been recognized for many years that some patients with reflux do not respond to proton pump inhibitors and continue to produce normal amounts of acid despite treatment.\(^16\)

Other otolaryngologists assume that if the patient has failed a therapeutic trial, the LPR is severe and requires even higher doses of PPI therapy, and the addition of other reflux or promotility medications which often are prescribed empirically (without tests objective for reflux).

At present, our field is in need of definitive, prospective, evidence-based studies. However, while we are awaiting such data, we might benefit from another consensus conference regarding appropriate clinical management with the technology available to us currently. The last such consensus conference statement was published in 1996.\(^17\) Many critical questions need to be addressed to guide clinical care. Among others, they include the following:

1. What constitutes normal acid exposure in the larynx?

The definition of “normal” pH monitor results remains controversial, and there are commonly differences in opinion between laryngologists and gastroenterologists regarding this important topic. Most of the support for laryngologic opinion is anecdotal, but such clinical judgments should be studied, not dismissed. Many laryngologists (this author among them) believe that in some patients, any laryngeal acid exposure can cause signs and symptoms, even occasional laryngeal acid contact that may occur only once every day or two (perhaps less). This seems intuitively plausible. If one were to place a single drop of gastric juice in an individual’s eye every day or two, that eye would probably remain erythematous and more prone to injury than the normal eye, if both eyes were traumatized by a foreign body such as sand, for example. There is no evidence that laryngeal mucosa is any more equipped to tolerate acid contact than the eye. While this hypothesis is probably true for some patients, it is important to recognize biologic variability, about which there is surprisingly little discussion in the LPR literature. Just as some patients smoke three packs of cigarettes a day for 60 years without developing cancer and others develop cancer after smoking just one pack a day for ten years, it is likely that laryngeal response to acid contact varies among individuals. This issue requires study; and it also requires consideration when interpreting results of LPR diagnostic studies, therapeutic response, and clinical trials, especially when sample size is small.

Despite the paucity of solid evidence, laryngologists have reached many of their opinions about LPR through...
considered clinical experience and meticulous patient observation. Unless/until beliefs grounded in the art of medicine are contradicted by evidence-based data, it is reasonable to consider clinical “wisdom” when considering protocols for diagnosis and treatment, but clinical judgments should be tested and augmented by data whenever possible. For example, the author has a growing number of patients who have had persistent symptoms and signs of reflux while using proton pump inhibitors, and whose 24-hour pH impedance monitors have shown continued acid production reaching the proximal sensor. Some of these patients improve with increased proton pump inhibitor therapy, others have continued to have symptoms and signs on four proton pump inhibitors a day and have responded to fundoplication. Interestingly, we also have had some successful fundoplication results in patients who remained symptomatic (positive symptom index) from non-acid reflux alone.

Many gastroenterologists remain uncomfortable with our interpretation of these findings and especially with the trend toward surgery. In general, if a gastroenterologist reads a 24-hour pH impedance study performed on medications that has four or five episodes of acid reflux at the proximal sensor, he/she will interpret the study as showing “normal acid exposure.”

The problem is that the normative data for pH studies were established in patients who had not been meticulously screened for extraesophageal reflux disease in general, or for LPR in particular. So many of the norms developed for patients with heartburn and using absence of heartburn as the primary control criteria may not be ideal for LPR patients. Clearly, the solution is expertly designed, collaborative studies involving laryngologists, gastroenterologists and comprehensive, individualized patient evaluation in order to determine the range of effects of acid exposure, and optimal management.

2. How should we diagnose LPR, and what constitutes an appropriate evaluation protocol?

Is a successful therapeutic trial of medication alone adequate? If it is adequate to establish a diagnosis of LPR (particularly if symptoms and signs return if the medicines are stopped), is control of acidity sufficient management for LPR? Gastroenterologists established criteria for esophageal screening based primarily on age and duration of heartburn. The criteria were selected to identify people at risk for Barrett’s esophagus and esophageal cancer. However, many LPR patients are young (well under 40) and have no heartburn; but they may have a 30-year history of reflux beginning at birth (or perhaps before birth). These patients may constitute an “at risk” population that falls outside the current guidelines for screening. Should they all undergo transnasal esophagoscopy (TNE), esophagogastroduodenoscopy (EGD), or some other physical examination? This author suspects that the standard of care will trend in that direction.

3. How should we manage patients who have persistent signs and symptoms (including those who have improvement but not resolution) following treatment with PPIs?

In the author’s experience, 24-hour pH impedance studies with symptom indices have proven invaluable and offer striking advantages over empirical management alone. Some patients require more than two PPIs a day to accomplish complete, or adequate, proximal acid suppression and improvement in symptoms and signs. Others have complete acid control, but persistent symptoms caused by non-acid reflux as confirmed by symptom index. Others appear to have symptoms and signs that are not causally related to reflux, and other causes must be sought. However, despite complete acid control, if they had documented reflux off medications, should they undergo esophagoscopy even if the documented reflux is not responsible for their laryngeal complaints?

**CONCLUSION**

LPR represents a complex spectrum of pathophysiology, diagnostic challenge and therapeutic controversy. Patient management can be optimized only through excellently designed studies with rigorous inclusion criteria, involving close collaboration among laryngologists, gastroenterologists, research scientists, and reflux surgeons. Considering the rapidly growing body of knowledge regarding reflux disease, the potentially serious consequences of undertreated reflux, the importance of other entities that may be missed when they are misdiagnosed as reflux, and considering the interdisciplinary collegiality that exists currently nationally and internationally, there is every reason to believe that it is possible to establish interinstitutional, unbiased collaboration that should provide answers to these important
clinical questions in the near future and that should lead to consensus regarding rational diagnosis of and treatment for laryngopharyngeal reflux. Singing teachers should be familiar with the complexities of this common disorder and with the frequently changing medical literature that guides diagnosis and treatment.

[Modified from Ear, Nose and Throat Journal, with permission from Vendome Group, L.L.C.]

NOTES


Robert T. Sataloff, MD, DMA is Professor and Chairman of the Department of Otolaryngology—Head and Neck Surgery and Senior Associate Dean for Clinical Academic Specialties at Drexel University College of Medicine. He is also on the faculty at Thomas Jefferson University, the University of Pennsylvania, Temple University, and the Academy of Vocal Arts. Dr. Sataloff served for nearly four decades as Conductor of the Thomas Jefferson University Choir and Orchestra, and is Director of The Voice Foundation’s Annual Symposium on Care of the Professional Voice. Dr. Sataloff is also a professional singer and singing teacher. He holds an undergraduate degree from Haverford College in Music Composition, graduated from Jefferson Medical College, received a DMA in Voice Performance from Combs College of Music, and completed his Residency in Otolaryngology—Head and Neck Surgery at the University of Michigan. He also completed a Fellowship in Otology, Neurotology, and Skull Base Surgery at the University of Michigan. Dr. Sataloff is Chairman of the Board of Directors of The Voice Foundation and of the American Institute for Voice and Ear Research. He is Editor-in-Chief of the *Journal of Voice*, Editor-in-Chief of the *Ear, Nose and Throat Journal*, an Associate Editor of the *Journal of Singing*, and on the Editorial Board of *Medical Problems of Performing Artists* and numerous major otolaryngology journals in the United States. Dr. Sataloff has written over 700 publications, including thirty-eight books. Dr. Sataloff’s medical practice is limited to care of the professional voice and to otology/neurotology/skull base surgery.

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I shot an arrow into the air,
It fell to earth, I knew not where;
For, so swiftly it flew, the sight
Could not follow it in its flight.

I breathed a song into the air,
It fell to earth, I knew not where;
For who has sight so keen and strong,
That it can follow the flight of song?

Long, long afterward, in an oak
I found the arrow, still unbroke;
And the song, from beginning to end,
I found again in the heart of a friend.

"The Arrow and the Song"
Henry Wadsworth Longfellow