It has been estimated that half of otolaryngology (ORL) patients with laryngeal and voice disorders have laryngopharyngeal reflux (LPR) as the primary cause or as a significant etiologic cofactor.1 This appears to be true for patients with diverse clinical manifestations.2-22 Many voice clinicians (including the authors) recommend that LPR be routinely assessed in patients with laryngeal and voice disorders; however, even among otolaryngologists who have a relatively high index of suspicion for LPR, it appears that this disorder is still often underdiagnosed and undertreated.22 There appears to be a four-part explanation:

1. The symptoms, manifestations, patterns, and mechanisms of LPR and gastroesophageal reflux disease (GERD) are different.2-4,22-35 Consequently, patients with LPR usually deny symptoms of heartburn and/or regurgitation.2-4,26,28 Fewer than half of ORL patients with LPR documented by pH monitoring complain of heartburn or regurgitation, symptoms that clinicians have traditionally felt must be present to diagnose reflux disease.2,4-26

2. The findings of LPR on laryngeal examination vary considerably, and laryngeal edema, a hallmark of LPR, is often unappreciated as a positive finding.36-38 Most otolaryngologists rely solely on the findings of erythema or of posterior laryngitis (red arytenoids and piled-up, hypertrophic, posterior commissure mucosa) as the diagnostic sine qua non of LPR. Unfortunately, those findings are not present in many LPR patients. In the authors’ experience, edema (and not erythema) is the principal, and most common, finding of LPR. The edema may be diffuse, or it may create the illusion of sulcus vocalis, an appearance that is the result of subglottic edema in Reinke’s space.38 When the edema involves both the true and false vocal folds, it may cause the laryngeal ventricles to swell shut. This relatively common finding is termed ventricular obliteration.

3. Traditional diagnostic tests for gastroesophageal reflux disease (GERD) lack both sensitivity and specificity for LPR. Barium esophagography, radionuclide scanning, the Bernstein acid-perfusion test, and esophagoscopy with biopsy are all often negative in LPR patients.3 This is probably because most LPR patients do not develop esophagitis, which is typically observed in gastroenterology patients with GERD.2,3,26-28 In addition, LPR is frequently intermittent, and exacerba-
tions depend to some extent on ever-changing dietary and lifestyle factors.

4. Therapeutic trials using traditional antireflux therapy often fail in LPR patients, so that clinicians may falsely conclude that LPR is not present. The traditional treatment for GERD, particularly in a patient with esophagitis, includes dietary and lifestyle modifications and use of antacids, H2-blockers, and/or single-daily-dose proton pump inhibitors (PPIs). Such treatment fails to control LPR in up to 50% of patients. In many cases, the treatment dose is inadequate (as most LPR patients require b.i.d. PPI treatment; also, the duration of the therapeutic trial is often too “short.” Many clinicians believe that a therapeutic trial of antireflux therapy of few weeks duration is adequate, but that is not the case. Patients with longstanding LPR often require 6 months or more of optimal treatment (acid suppression) with PPI to resolve their symptoms and findings. Also, PPI resistance in LPR patients is not uncommon, being about 10%. Within the last two decades, with the availability of new diagnostic methods and treatments, researchers have begun to elucidate the clinical patterns and mechanisms of LPR. It now appears that patients with LPR are quite different from typical gastroenterologist’s model of GERD, and esophagitis (ie, GERD). How are LPR patients different than those with GERD? Why do ORL patients usually deny heartburn? What are the differences in the mechanisms of LPR and GERD? Previously, the diagnosis of LPR was erroneously based on the gastroenterologist’s esophagitis model of GERD. Improved diagnostic technology and effective treatments are beginning to yield important information about LPR and how it differs from GERD.

In a relative sense, ambulatory 24-hour double-probe (simultaneous esophageal and pharyngeal) pH monitoring (pH-metry) has become the diagnostic gold standard for LPR; however, as a diagnostic, it is expensive and it is not widely available. Nevertheless, pH-metry effectively documents LPR with a high degree of specificity and sensitivity. The next tier of reflux-testing, impedance, may prove to be even better for diagnosis in certain LPR subgroups, such as those with a chief complaint of chronic cough.

Transnasal esophagoscopy (TNE) is performed in the clinic setting without anesthesia or sedation (other than topical numbing of the nose). TNE has allowed the otolaryngologist to screen the esophagus. In a large series, Postma et al reported that 50% of the patients had positive findings on TNE, including, esophagitis 17%, hiatal hernia 8%, Barrett’s metaplasia 5%, candida esophagitis 5%, and stricture 4%.

The treatment of LPR took a giant leap forward with the introduction of proton pump inhibitors (PPIs) into the United States in 1989. Compared to previous treatments, PPIs more effectively reduce gastric acid production. In addition, antireflux surgery has been shown to be very effective for patients with recalcitrant or life-threatening LPR.

**HOW AND WHY ARE ORL PATIENTS WITH LPR DIFFERENT FROM GI PATIENTS WITH GERD?**

Ossakow et al compared the symptoms and findings of reflux disease in two discrete groups: ORL patients (n = 63) and GI patients (n = 36). They reported that hoarseness was present in 100% of the ORL patients and 0% of the GI patients and that heartburn was present in 89% of the GI patients, but in only 6% of the ORL patients. Other authors also have reported a low incidence of heartburn as a symptom in ORL patients with LPR. Heartburn is a symptom of esophagitis, and most ORL patients do not have esophagitis. Wiener et al studied 32 ORL patients with hoarseness and found that although pH-metry was abnormal in 78%, esophageal manometry was normal in 100%, and esophagoscopy with biopsy was normal in 72%. Koufman found that fewer than 20% of ORL patients with LPR had findings of esophagitis by TNE or barium esophagogram. By comparison, esophagitis is found in most GI patients.

It may seem counterintuitive that LPR patients do not also have GERD, and this is an important reason why some clinicians remain skeptical of the diagnosis LPR. It is hard for some people to believe that one could have reflux-related disease without having heartburn or regurgitation. The explanation lies in examination of the pathophysiology of the two conditions; the mechanisms of LPR and GERD differ significantly. Both LPR and GERD are caused by mucosal injury from acid and pepsin exposure. Esophageal epithelium, however, has protective mechanisms that make it more resistant to peptic injury that of the laryngopharynx. Furthermore, it is important to recognize that pepsin and not acid produces most reflux-related tissue injury or damage.

Research is now exploring the cell biology of LPR, and it confirms that mucosal damage from pepsin is related to depletion of important cellular defense-proteins, such as carbonic anhydrase, E-cadherin (the material that makes up the “mortar” between squamous epithelial cells, the tight junctions), COX-2, and the stress proteins. In addition, it takes much less acid/pepsin exposure to cause tissue damage in the pharynx and larynx than in the esophagus. Thus, even patients without enough esophageal reflux to de-
velop esophagitis (and its principal symptom heartburn) still may develop symptomatic LPR.

The clinical manifestations and findings of reflux disease are different in GI and ORL patients, because the mechanisms of GERD and LPR are different. Usually, GI patients have esophageal dysmotility and lower esophageal sphincter (LES) dysfunction, whereas ORL patients generally have good esophageal motor function, but faulty upper esophageal sphincter (UES) function.3,29,34

GI patients with GERD experience abnormal nocturnal (supine) esophageal reflux, but only uncommonly experience daytime (upright) reflux; in contrast, LPR patients experience abnormal daytime upright reflux, but not supine nocturnal reflux.1-3 Not surprisingly, esophageal motility is more frequently abnormal in GI patients than in ORL patients.29 In addition, it has been shown experimentally that instilling acid in the distal esophagus of normal subjects and of patients with esophagitis usually results in a prompt increase in tone of the UES.31 This physiologic response does not appear to be intact in ORL patients with LPR.

In summary, it appears that significant differences in esophageal (dys)function and reflux pattern may explain many of the clinical differences between LPR and GERD. Table 28–1 summarizes those differences.

### CLINICAL MANIFESTATIONS OF LPR

In a large series of patients with LPR, dysphonia (hoarseness) was found to be the most common symptom (92%).3 The pattern of dysphonia was either chronic or intermittent. Patients with intermittent dysphonia often complained that they suffered from “laryngitis” that lasted for days or weeks, several times a year.3 Additional symptoms were experienced by the majority of the patients: chronic throat clearing (50%), chronic cough (44%), globus (33%), and dysphagia (27%). More than half the patients denied having any heartburn whatsoever; 13% had two or fewer episodes per week, and only 10% complained of more frequent or daily heartburn.3

Although most patients with LPR present with mild to moderate dysphonia as the primary symptom, some suffer from more serious, even life-threatening, conditions (Table 28–2). Other laryngeal manifestations of

<table>
<thead>
<tr>
<th>Table 28–1. Typical Differences Between LPR and GERD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
</tr>
<tr>
<td>Heartburn and/or regurgitation</td>
</tr>
<tr>
<td>Hoarseness, cough, dysphagia, globus</td>
</tr>
<tr>
<td><strong>Findings</strong></td>
</tr>
<tr>
<td>Esophagitis</td>
</tr>
<tr>
<td>Laryngeal inflammation</td>
</tr>
<tr>
<td><strong>Test results</strong></td>
</tr>
<tr>
<td>Esophageal biopsy (esophagitis)</td>
</tr>
<tr>
<td>Abnormal esophageal manometry</td>
</tr>
<tr>
<td>Abnormal esophageal pH monitoring</td>
</tr>
<tr>
<td>Abnormal pharyngeal pH monitoring</td>
</tr>
<tr>
<td><strong>Pattern of reflux</strong></td>
</tr>
<tr>
<td>Supine (nocturnal)</td>
</tr>
<tr>
<td>Upright (awake)</td>
</tr>
<tr>
<td><strong>Response to treatment</strong></td>
</tr>
<tr>
<td>Dietary and lifestyle modifications</td>
</tr>
<tr>
<td>Success with H2-blockers</td>
</tr>
<tr>
<td>Success with proton pump inhibitors (PPIs)*</td>
</tr>
</tbody>
</table>

GERD = Gastroesophageal reflux disease
LPR = Laryngopharyngeal reflux

*Assuming adequate dosage and duration of therapy, i.e., b.i.d. PPIs for LPR.

Table data derived from Koufman.2
LPR include laryngospasm, 20-22 laryngeal stenosis, and carcinoma.12,21 LPR is also associated with the development of polypoid degeneration (Reinke’s edema), vocal nodules, and functional voice disorders.1,13-19

Reflux and Functional (“Nonorganic”) Voice Disorders

The term functional voice disorder (FVD) applies to a variety of vocal abuse, misuse, or overuse syndromes. These conditions are also called muscle tension dysphonias (MTDs), because transnasal fiberoptic laryngoscopy (TFL) shows consistently abnormal patterns of laryngeal biomechanics. The most commonly observed pattern is supraglottic contraction, either anteroposterior contraction (foreshortening of the vocal folds) and/or false vocal fold approximation/compression.11

The FVD group of conditions is often associated with the secondary development of histopathologic changes of vocal folds, which include hematomas, nodules, ulcers, cysts, pseudocysts, granulomas, and Reinke’s edema. With the availability of pH-metry, data suggest that 70% of patients with these functional lesions have LPR in addition to abnormal laryngeal biomechanics.1

As part of the evaluation of each patient with an FVD, the clinician should elicit a reflux history. In addition, patients who have laryngeal erythema, edema, or thick mucus in the endolarynx should be suspected of having LPR. Although the treatment of LPR alone will not resolve most FVDs, some cases will resolve. Certainly, failure to treat LPR, when it is present, will delay or prevent resolution of the FVD.

It is important to note that the laryngeal findings of LPR may be subtle in the face of significant supraglottic contraction. The appearance of a (subglottic) groove giving each of the vocal folds the appearance of a sulcus (pseudosulcus)38 should alert the clinician to the possibility of LPR. Likewise, the presence of thick endolaryngeal mucus is often a sign of LPR. This finding is probably the result of a local tissue inflammatory response to chronic irritation and not “postnasal drip.”

Granulomas

The etiology of granulomas of the vocal process is multifactorial, but LPR is almost always a cofactor. Granulomas usually result from the combination of acute mucosal ulceration of the vocal process, LPR, and chronic vocal trauma caused by throat clearing and/or a hard glottal attack.16,17 By itself, chronic vocal trauma can lead to vocal fold ulcers and granulomas; however, in the majority of cases, LPR is a cofactor. The clinician should, in each case, consider each of the possible contributing etiologic factors and correct each if therapy is to be effective. In the case of granulomas, effective antireflux therapy is sufficient to allow healing in the majority of patients within 8 months, as long as vocally abusive behaviors also are corrected.16,17

Paroxysmal Laryngospasm

Laryngospasm is an uncommon complaint, but patients who experience this frightening symptom are usually able to describe events in vivid detail.3 If the clinician mimics severe inspiratory stridor, the patient will confirm that his or her breathing during an attack...
does indeed sound similar. Some patients are aware of a relationship between LPR and laryngospasm, others are not.\(^7\)

In a canine model, Loughlin et al\(^8\) showed that chemoreceptors (“taste buds”) on the epiglottis responded to acid stimulation at pH of 2.5 (or lower) by triggering reflex laryngospasm. The afferent limb of this reflex is supplied by the superior laryngeal nerve, and nerve interruption abolished the laryngospasm reflex.\(^8\)

In the authors’ experience, the majority of patients with paroxysmal laryngospasm respond well to PPI therapy. Antireflux surgery (fundoplication) may be necessary in patients who fail medical treatment.\(^47\) LPR-related laryngospasm may also be related to (or a cause of) the sudden infant death syndrome (SIDS).\(^6,9\)

### Polypoid Degeneration (Reinke’s Edema)

Polypoid degeneration results from chronic laryngeal irritation over a period of many years. It is almost always bilateral and occurs most frequently in elderly female smokers. It is also seen in nonsmoking patients with LPR or hypothyroidism.

Polypoid degeneration may improve with antireflux therapy and cessation of smoking, but most patients with these lesions will require concomitant surgical treatment. Most patients with polypoid degeneration have abnormal pH-metry.\(^1\) Consequently, LPR should be considered a key component in the pathogenesis of this condition, and patients undergoing surgical therapy should receive intense antireflux treatment for several months prior to surgery and during the perioperative period. This usually will help avoid surgical complications.\(^18\)

### Laryngeal Stenosis

Excluding trauma, LPR is the primary cause of subglottic and posterior laryngeal stenosis.\(^3,20\) Chronic, intermittent, or chronic-intermittent LPR can cause, or indefinitely perpetuate, a laryngeal disorder. Using a canine model, it has been shown that intermittent (three times per week only) applications of acid and pepsin to the subglottic region following mucosal injury results in nonhealing ulceration of the cricoid, and even subglottic stenosis.\(^3,20\) LPR documented by pH-metry has been found in 92% of stenosis cases.\(^3\) In the authors’ experience, intensive antireflux treatment (with PPIs or fundoplication) is highly successful in leading to decannulation in the majority of patients with stenosis.

The traditional dichotomy between mature and immature stenoses probably represents an oversimplification. Immature implies that massive edema and granulation tissue are present and that the inflammatory process is ongoing. Mature implies that acute inflammation has resolved, and that the stenosis is composed of mature fibrous tissue with thin (normal) overlying epithelium. Surgical attempts to correct immature stenosis usually fail unless the underlying inflammatory process is controlled. Conversely, mature stenoses are more often successfully corrected. In reality, many cases are neither mature nor immature, but somewhere in between. The same also may be true of many acquired laryngeal webs. In the authors’ opinion, pH-metry and tight LPR control are indicated in all stenosis cases.

### Carcinoma of the Larynx

The most important (identified) risk factors for the development of laryngeal carcinoma are tobacco and alcohol; however, LPR also appears to be an important cofactor, especially in nonsmokers.\(^3,12,21\) The senior author reported 50 consecutive cases of laryngeal carcinoma in which LPR was documented in 84%, but only 58% were active smokers. The exact relationship between LPR and malignant degeneration remains to be proved, but the available pH-metry data suggest that most patients who develop laryngeal malignancy both smoke and have LPR. In addition, leukoplakia and other premalignant appearing lesions may resolve with antireflux therapy.

Tobacco and alcohol adversely influence almost all the body’s antireflux mechanisms—they delay gastric emptying, decrease lower esophageal sphincter pressure and esophageal motility, decrease mucosal resistance, and increase gastric acid secretion—and thus, strongly predispose one to reflux. pH-metry, followed by rigorous antireflux treatment, is recommended for all patients with laryngeal neoplasia, with or without other risk factors. Treatment for this group of patients probably should be lifelong.

### Diagnosis

When a patient presents with dysphonia, globus, dysphagia, chronic throat clearing and cough, or complaints of “too much throat mucus,” symptoms that suggest LPR, the clinician should perform a complete otolaryngologic examination, fiberoptic laryngoscopy, and consider pH-metry or impedance testing as well as a screening examination of the esophagus (ie, transnasal esophagoscopy).

The reflux symptom index (RSI)\(^23\) and the reflux finding score (RFS)\(^36\) are also useful in the assessment...
process, especially after initiation of therapy. Both indices have been shown to be good treatment outcome measures.\textsuperscript{23,36,37}

At present, double-probe pH-metry and impedance testing have tremendous advantages over any other diagnostic method, because they are both highly sensitive and specific.\textsuperscript{3,24,25} Furthermore, they reveal the pattern of reflux, so that subsequent treatment can be custom-tailored for each patient.\textsuperscript{3} For example, if the patient does not have supine nocturnal reflux, then elevation of the head of the bed need not be recommended.

pH metry has been available for many years, and standards (normal values) have been established in many laboratories.\textsuperscript{1,2,5,24,25} For the esophageal probe, the most important parameter is considered to be the percentage of time that the pH is less than 4, and this measurement is usually recorded for time in the upright position, time in the supine position, and the total time of the study.\textsuperscript{2,24,25} For the upright period, the upper limit of normal is approximately 8.0\% and for the supine, approximately 2.5\%.\textsuperscript{2,29,30} However, in many patients (especially professional voice users), lesser exposures may be associated with clinical symptoms.

The Pharyngeal Probe is Essential in Diagnosing LPR

Pharyngeal (double-probe) pH monitoring, with the second (proximal) probe being placed just above the criopharyngeus, when positive, is by definition diagnostic of LPR.\textsuperscript{3,24} At our institutions, and at most others doing such testing, any pharyngeal acid exposure is considered to be abnormal.\textsuperscript{3} Figure 28–1 shows an example of a portion of a double-probe pH study in which reflux is seen in both the esophageal and the pharyngeal probes.

Double-probe pH-metry is particularly important in ORL patients because the diagnosis of LPR can be missed in a patient with a “normal” esophageal study. It has been shown that the sensitivity of single-probe esophageal pH monitoring for LPR is only 62\%, and its positive predictive value only 49\%.\textsuperscript{48} Were it not for the pharyngeal probe findings, many LPR patients would escape physical detection. Pharyngeal pH monitoring is necessary in ORL/LPR patients because it dramatically increases the diagnostic accuracy and is an effective method to assess therapeutic efficacy.

Screening Examinations of the Esophagus

Patients with significant LPR should have a screening examination of the esophagus. Although a barium esophagram is not a sensitive test for diagnosing LPR, it may be useful in patients with primary complaints of globus and/or dysphagia. Otherwise, unsedated, in-office, transnasal esophagoscopy (TNE) is recommended.\textsuperscript{26-28} In a series of more than 700 patients undergoing such TNE, half had some esophageal abnormality, such as esophagitis, stricture, hiatal hernia, or Barrett’s esophagus.\textsuperscript{28}

Figure 28–2A shows the appearance of a peptic stricture that was an incidental finding. The patient presented with dysphonia, chronic throat clearing, cough, and dysphagia. He had grossly abnormal pH-metry (upright and supine). A biopsy of the esophagus was recommended, but the patient refused. He
was treated with omeprazole 20 mg b.i.d. and after 3 months was asymptomatic. A repeat barium examination, performed 5 months after the initial study, showed that the stricture had almost resolved (Figure 28–2B).

On the horizon, there are LPR diagnostics that rely on identification of pepsin and other markers of LPR in tissues and/or airway secretions. In other words, some day, analysis of sputum will provide diagnostic information about the health and disease of the aero-digestive tract.

**TREATMENT**

The treatment of acid-related disorders has evolved over time, often following the development of new medications. Initial treatment regimens relied on dietary and lifestyle changes and the administration of antacids. Such regimens were only minimally effective in treating LPR. With H2-receptor antagonists, the results of treatment of these disorders improved. Studies demonstrate that about 50% of LPR patients improve on H2-blockers, leaving a significant proportion of patients without benefit. This is largely caused by the inability of this class of medication to inhibit meal-stimulated acid secretion.

Proton pump inhibitors (PPIs) are more effective, and these drugs directly target H+\(\text{-}\)K+ ATPase, the key enzyme in the final acid production pathway within the parietal cell. The elimination or marked suppression of acid production accomplished two things: it reduced exposure of damaged tissues to an acidic environment and, perhaps more importantly, it reduced the activity of pepsin, which requires hydrogen ions (acid) for activation.

Clinical trials have confirmed the superiority of PPIs to H2-blockers both in symptom relief and in mucosal healing. Because PPIs act at the final pathway of acid production, as opposed to H2-blockers, which modulate acid output through blocking stimulation of the parietal cell, PPIs have the ability to more completely suppress acid production (basal and meal-stimulated).

PPIs have been particularly effective in improving the healing rate in patients with LPR. As discussed...
above, the larynx is far more susceptible to injury from refluxate than the esophagus.° Optimal treatment of LPR therefore requires near complete cessation of acid-pepsin injury if healing is to occur.22

PPIs are not effective in all reflux patients, especially with once-daily dosing. Studies done on once-a-day dosing have demonstrated significant failure rates.41,42 Other studies have demonstrated that the average morning dose of PPI lasts an average of only 13.8 hours,43 and that the evening dose lasts just 7.5 hours.43 There have been reports of LPR treatment failures, even on high-dose PPI therapy42,43; we found a medical treatment failure rate of 10% in LPR patients receiving only PPIs.42

In contrast to GERD, the symptoms of patients with LPR do not resolve in days or weeks; often it takes several months for resolution to occur.3,22 One follow-up study revealed that fewer than half of patients treated with PPIs are completely well (all symptoms and findings resolved) by 4 months of treatment.46 Despite the fact that they are not completely effective in all patients, PPIs are still considered the standard therapy for patients with moderate to severe findings or complications of LPR.10

For reasons mentioned above, a minimum of twice-daily dosing is recommended for LPR. The medication should be taken when the patient arises in the morning and late in the afternoon, prior to the evening meal. Finally, the recommended duration of initial therapy with PPIs should be 6 months.22

**Therapeutic Algorithms**

When treating patients with LPR, the severity of the symptoms and findings, the presence of neoplastic lesions, the potential for development of life-threatening complications, the response to previous therapy, the results of pH-metry, the age and occupation of patient, the presence of comorbidities, and compliance issues all influence management. In addition, consideration must be given not only to initial treatment but also to long-range management.

**Treatment of Mild to Moderate LPR**

For many otolaryngologists, this group comprises the majority of patients with LPR. Such patients typically present with symptoms of intermittent dysphonia, chronic throat clearing, globus pharyngeus, and dysphagia, and findings such as laryngeal edema and posterior laryngitis. It is appropriate for the otolaryngologist to adopt a less aggressive approach to the management of patients in this group. It is not essential to obtain pH-metry routinely in such patients prior to treatment. Initial treatment may be with H2-blockers, antacids, and dietary and lifestyle modifications. The latter include: smoking cessation, weight reduction, avoidance of overeating and late night meals, a low-fat diet, and avoidance of known reflexogenic foods, such as coffee, chocolate, mints, and soda.

Anti-reflux and anti-acid therapy has two simultaneous goals: to arrest the inflammatory process in the larynx by eliminating the presence of gastric acid and, if possible, to reconstitute the body’s normal antireflux defenses. The initial 6-month period of medical therapy should be used to optimize reversible risk factors that are within the patient’s control. Some patients report, for example, that LPR seems to decrease significantly when their weight is close to ideal or with smoking cessation.

The combination of dietary and lifestyle modifications, antacids, and H2-blockers is seldom as effective as desired. But, if that regimen fails, the patient should be placed on a PPI, starting at a twice-daily dose. The dose of the PPI may also be escalated to achieve a therapeutic response, and adequate time must be given for healing to occur.

There are patients who will appear to be failing high-dose PPI therapy. Such nonresponders should undergo pH-metry while on medication to evaluate drug efficacy. If the patient fails this study, the dose or type of PPI may be adjusted, or a referral made for fundoplication.47 Medical treatment should be continued for a minimum of 6 months. If the patient becomes asymptomatic after this interval, medication may be decreased or discontinued. However, it is important to counsel patients prior to decreasing or terminating treatment that LPR may relapse. Many patients have disease-free intervals of months or years, but eventually suffer recurrences. Some LPR patients will need lifetime treatment.

The chronic-intermittent pattern of LPR requires the clinician to individualize treatment. Some relatively asymptomatic LPR patients, especially professional vocalists, will need close, long-term follow-up.

After 6 months of therapy, the PPI dose may be tapered. An H2-blocker is prescribed to prevent rebound acid reflux in the tapering period. Patients should be warned that they may experience a recrudescence of symptoms for a few days following cessation of the PPI. All patients should be re-examined after 6 to 8 weeks, and if the patient has recurrent symptoms or findings, an appropriate treatment regimen should be reinstated.

**Treatment of Moderate to Severe LPR**

Ideally, all patients with laryngeal carcinoma, acquired webs and stenoses, and laryngospasm should under-
go pH-metry before treatment is initiated; however, this is not always possible, particularly if the patient requires emergency surgical treatment such as tracheotomy. Nevertheless, every effort should be made to obtain pH-metry prior to treatment in this group of patients because: (1) it establishes the diagnosis of LPR; (2) it determines the severity of the LPR (and establishes a baseline); (3) it allows treatment to be individualized; and (4) it may justify unconventional treatment (eg, early fundoplication). For similar reasons, an examination of the esophagus should be performed.

The minimum initial treatment in these patients should be with a PPI at a twice-daily dose and dietary and lifestyle modifications. A t.i.d. starting dose may be advisable for patients weighing over 200 pounds. Optimal dosing can be adjusted using pH-metry in individuals who do not appear to be responding to treatment. In the event that the patient is unable to take orally administered medicine, an intravenous ranitidine drip should be employed, and the gastric contents should be neutralized using antacids if the patient's stomach is intubated.

In selected cases, those with the most severe form of LPR, particularly young patients (under 40 years of age), fundoplication should be considered as an early alternative. If, for example, a young person presents with subglottic stenosis and laryngeal airway obstruction, with no prior history of trauma or intubation, and pH evidence of severe LPR with a very low LES pressure (less than 6 mm Hg) on manometry, fundoplication may be an advisable alternative to medical treatment.

For most patients, PPIs are the treatment of choice for the first 6 months, or until the clinical situation that prompted the intervention has resolved. For example, it is invidious to stop the PPI in laryngeal stenosis patients still being treated for the stenosis. As some of these patients present with airway obstruction severe enough to require tracheotomy, PPI treatment should be continued until the patient has been successfully decannulated and it is clear that the LPR is under control, the latter being confirmed by repeat pH-metry. In practice, most patients with stenosis will require either chronic PPI therapy or fundoplication. The same is true for many patients with carcinoma of the larynx, especially nonsmokers who develop carcinoma. In this group, the risk of the patient developing new neoplastic lesions exceeds the risks of definitive long-term antireflux treatment.

When omeprazole (the first PPI) was introduced in the United States in 1989, the Food and Drug Administration recommended that it be used in a dose of 20 mg per day for only 6 to 8 weeks. This conservative recommendation was made because omeprazole in large doses for a prolonged period had been shown to produce carcinoid tumors in laboratory animals. It was soon clear that this regimen was woefully inadequate to treat many LPR patients. Fortunately, long-term PPI therapy has been studied extensively in Europe. It is now clear that these drugs are safe and that they must be employed in larger doses and for prolonged periods.

In patients with LPR over the age of 60 years, chronic, long-term, twice-daily PPI treatment is recommended. On the other hand, if the patient has only supine or upright reflux disease, and not both, a single daily dose may suffice for maintenance after the acute phase of the illness has resolved. However, considerable variability is seen, and treatment must be individualized.

For patients under 40 years of age requiring long-term antireflux therapy, fundoplication is often considered. For patients between the ages of 40 and 60 years, treatment is selected on an individual basis. In this group, the severity of LPR and the underlying condition are considered, as well as the preferences and overall medical condition of the patient.

Fundoplication as a surgical antireflux treatment is highly effective; however, it does appear to require special technical expertise. Surgical antireflux procedures are a real therapeutic option for some patients, particularly young patients with severe reflux disease. Fundoplication is often recommended for patients with subglottic and tracheal stenosis, as this group appears to have a very high failure rate with medical treatment and a high likelihood of developing recurrent airway problems later on if medical treatment subsequently fails. Laparoscopic fundoplication has proved highly successful and eliminates much of the morbidity associated with the traditional approach.

SPECIAL CONSIDERATIONS

LPR in Pediatric Patients

Pediatric patients also suffer from LPR. Dysphonia, laryngospasm, laryngomalacia, and pulmonary disorders, such as asthma, have been shown to be related to reflux in infants and children. Experimental data also suggest that SIDS may be reflux-related. Diagnostic pH-metry is especially useful in pediatric patients, because they seldom complain of reflux symptoms, and because so little is known about LPR in the pediatric population. For pediatric patients with severe
of life-threatening complications of LPR, we recommend the use of PPIs. If there is evidence of medical treatment failure, the patient should be retested while on treatment. If the repeat pH-metry is abnormal, then fundoplication may be indicated.

**Xerostomia and LPR/GERD**

Xerostomia is often encountered in otolaryngologic practice. In addition to being common after irradiation, xerostomia is also seen with Sjögren’s syndrome, scleroderma, most other collagen vascular diseases, cystic fibrosis, and with the use of many medications (eg, anticholinergics, antihypertensives, antihistamines). Xerostomia is a major contributing factor in the development of complications of reflux disease, both LPR and GERD. This is because salivary bicarbonate is needed to restore the intraluminal esophageal pH after a reflux episode. Without normal saliva, the esophageal pH remains very low for an extended period of time. In normal people, the process of pH neutralization takes several swallows (3–5 minutes) following the initial reflux event. In patients with xerostomia, each reflux episode (physiologic or otherwise) is associated with a prolonged period of esophageal acid exposure.

Korsten et al studied 16 patients with xerostomia caused by head and neck irradiation or medication. All had normal esophageal motility; however, pH-metry and esophageal acid clearance were markedly abnormal in these patients. In addition, the findings of esophagitis were significantly more common in the xerostomia group compared with controls, suggesting that salivary bicarbonate is critical to preventing mucosal damage.

**Surgery for Vocal Process Granulomas**

Surgical removal of vocal process granulomas is often an exercise in futility, as these lesions usually recur. As mentioned above, most are the result of both LPR and chronic vocal process trauma. The majority of these lesions resolve within 8 months with antireflux (PPI) therapy and with good vocal hygiene (correction of vocally abusive behaviors). Surgical removal of granulomas is, however, indicated in four situations:

1. When granulomas cause airway obstruction (uncommon).
2. When carcinoma is suspected (for biopsy). The majority of vocal process granulomas appear as smooth, shiny, bilobed, gray-white masses on the arytenoids. When a granuloma appears to spread anterior to the vocal process or takes on a ragged, keratotic appearance, the possibility of carcinoma must be entertained, and excisional biopsy is indicated.
3. When granulomas mature and become fibroepithelial polyps. On occasion, after an extensive period of treatment, a granuloma may take on the appearance of a mature, pedunculated, fibroepithelial polyp. When this occurs, additional medical treatment often fails to eradicate the lesion, and it should be excised.
4. To restore the voice in selected cases. Uncommonly, large granulomas may produce severe dysphonia. Removal may be indicated in selected cases in which the patient needs to use his or her voice for professional purposes.

**Timing of Surgery for Reinke’s Edema, Vocal Nodules, Cysts, and Papillomas**

Few patients with benign vocal fold lesions require emergency surgery, and many patients with vocal fold lesions also have LPR. It behooves the otolaryngologist to aggressively treat LPR prior to surgery. The authors recommend that antireflux therapy (double-dose PPI) should be instituted a minimum of 2 to 6 months prior to elective vocal fold surgery, and treatment should be continued postoperatively until healing is complete and normal stroboscopy has returned. The routine use of perioperative antireflux therapy, in our experience, appears to decrease postoperative complications of laryngeal surgery (eg, web information in papilloma patients).

**SUMMARY**

LPR is an elusive, ubiquitous, and pernicious cause of laryngeal inflammatory and neoplastic disorders; and, it appears to be clinically distinct from classic GERD. Frequently underdiagnosed and undertreated, LPR is believed to be an etiologic factor in most patients with laryngeal and voice disorders. The pervasive and serious nature of LPR demands that clinicians caring for patients with upper aerodigestive tract (especially laryngeal) disorders consider this diagnosis as a possibility in almost every case.

**REFERENCES**

2. Wiener GJ, Koufman JA, Wu WC, Cooper JB, Richter, JE, Castell DO. Chronic hoarseness secondary to gastroesophageal reflux disease: documentation with 24-h am-


