

**Shoib Sana, DO;**  
**Munib Sana, MD;**  
**Nikki Johnston, PhD;**  
**Sumeet K. Mittal, MD**  
Otolaryngology – Head  
and Neck Surgery, Detroit  
Medical Center, Detroit  
(Dr. Shoib Sana);  
Department of Radiology,  
Maine Medical Center,  
Portland (Dr. Munib Sana);  
Department of  
Otolaryngology and  
Communication  
Sciences, Medical College  
of Wisconsin, Milwaukee  
(Dr. Johnston); Esophageal  
Center, Creighton  
University School of  
Medicine, Omaha, Neb  
(Dr. Mittal)

✉ Ssana@dmc.org

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# Hoarseness and chronic cough: Would you suspect reflux?

Laryngopharyngeal reflux disease is often misdiagnosed as an upper respiratory infection or allergic rhinitis—or confused with GERD. This review will help you diagnose and treat it.

## PRACTICE RECOMMENDATIONS

➤ *Recommend dietary and behavioral modifications as a first step in treating patients with symptoms suggestive of laryngopharyngeal reflux disease (LPRD).* **C**

➤ *When medications are needed, prescribe a high-dose proton-pump inhibitor, a histamine-2 blocker at bedtime, and prophylactic antacids for reflux-inducing activities, such as exercising and eating.* **B**

➤ *Avoid the rebound effect associated with abrupt cessation of medications prescribed for LPRD with a gradual, 16-week taper.* **C**

### Strength of recommendation (SOR)

- A** Good-quality patient-oriented evidence
- B** Inconsistent or limited-quality patient-oriented evidence
- C** Consensus, usual practice, opinion, disease-oriented evidence, case series

**CASE ▶** When Joan C, a 35-year-old patient whom you've known for years, comes in for a physical, you notice that she's coughing frequently. Upon questioning, Joan says she first noticed the cough several months ago; she also reports that she's frequently hoarse, but has no other symptoms. Joan is a former smoker, and quit 4 years ago.

If Joan were your patient, would you suspect that she had an upper respiratory infection and prescribe an antibiotic such as azithromycin? Would you include laryngopharyngeal reflux disease in the differential diagnosis?

**L**aryngopharyngeal reflux disease (LPRD) is a common condition that most primary care physicians encounter frequently. It is also frequently misdiagnosed by clinicians who are unfamiliar with the differences between LPRD and gastroesophageal reflux disease (GERD).

The American Academy of Otolaryngology–Head and Neck Surgery defines laryngopharyngeal reflux as the retrograde movement of gastric contents into the laryngopharynx.<sup>1</sup> Common symptoms include hoarseness/dysphonia, chronic throat clearing, dysphagia, globus pharyngeus, and chronic cough, as well as postnasal drip, paroxysmal laryngospasm, odynophagia, excessive throat mucus, and a strange taste in the mouth.<sup>2</sup>

The diversity and vagueness of these symptoms, as well as the lack of a gold standard diagnostic test for LPRD, make it difficult to estimate its prevalence. In addition, signs of gastroesophageal reflux can be found in the laryngopharynx of up to 86% of healthy individuals, further complicating the clinical picture.<sup>3</sup> To avoid missing this often overlooked reflux disease, you need to know how it develops, what signs and symptoms to look for, and which distinguishing features to keep in mind.

TABLE 1

When to suspect laryngopharyngeal reflux disease<sup>1,5,24</sup>

Finding	Frequency among patients with LPRD (%)*
Dysphonia/hoarseness (intermittent)	71
Chronic cough	51
Globus pharyngeus	47
Chronic throat clearing	42
Dysphagia	35
Heartburn	35

\*The frequency of other symptoms associated with LPRD is not known.

### Pathophysiology and distinguishing features

The precise way in which LPRD develops is not known, but there are 2 proposed means of laryngeal injury—direct and indirect. In the first case, chemical irritants in the gastric refluxate enter the laryngopharynx and cause local mucosal injury. In the second, gastric reflux irritates the esophageal tissue enough to evoke laryngeal reflexes without ever reaching the larynx—a vagally mediated response associated with symptoms such as chronic cough, throat-clearing sensations, and bronchoconstriction.<sup>4</sup>

Unlike the esophageal lining, laryngeal epithelium is not protected against chemical injury from gastric acid, as it lacks both the stripping motion of esophageal peristalsis and the neutralizing bicarbonate in saliva.<sup>4</sup> Thus, while far smaller amounts of gastric reflux make it into the laryngopharynx, the acid remains there longer and may cause greater injury.<sup>5</sup> In some cases, this occurs as often as 50 times a day, although as few as 3 episodes per week have been known to cause LPRD.<sup>5</sup>

#### Heartburn is not the rule

Heartburn is a primary complaint of patients with GERD. It is reported by little more than a third (35%) of those with LPRD,<sup>5,6</sup> however, (which is why it is sometimes called the “silent” reflux disease). This is because heartburn is caused by esophagitis due to esophageal dysmotility and lower esophageal sphincter dysfunction,<sup>3</sup> while most patients with LPRD have normal esophageal motor

function and upper esophageal sphincter dysfunction. The fact that only a minimal amount of reflux enters the laryngopharynx may be part of the reason heartburn is less likely in patients with LPRD.

■ **Onset of symptoms.** When reflux occurs is another thing that distinguishes LPRD and GERD. Symptoms of GERD typically worsen when the individual is supine, while laryngopharyngeal reflux usually occurs when he or she is upright.<sup>7</sup> The frequency with which these 2 conditions overlap is debatable, as there are few studies differentiating LPRD and GERD based on standardized signs and symptoms.<sup>7</sup>

#### Making sense of signs and symptoms

Most patients with LPRD seek treatment from their primary care physician, typically reporting symptoms that they don't associate with gastric reflux, such as hoarseness, a chronic cough or sore throat, or the sensation of a lump in the throat (TABLE 1). Less common manifestations include “water brash”—excessive mucus in the mouth caused by a release of salivary bicarbonate to help neutralize acidity<sup>8</sup>—otitis media, sinus disease, and dental caries.<sup>5</sup>

■ **Laryngeal endoscopy** may reveal many changes from diffuse irritation. Diffuse erythema, edema, and interarytenoid hypertrophy/cobblestoning are the most useful findings for an LPRD diagnosis.<sup>9,10</sup> But in most cases, only a few nonspecific signs with



The timing of reflux—whether it occurs when the patient is standing or supine—can aid in differentiating between LPRD and GERD.

**TABLE 2**  
**Recommend these lifestyle  
 modifications<sup>19</sup>**

Stop smoking
Avoid: <ul style="list-style-type: none"> <li>• alcohol</li> <li>• caffeine</li> <li>• carbonated beverages</li> <li>• chocolate</li> <li>• citrus fruits</li> <li>• spicy/acidic foods</li> </ul>
Eat smaller, more frequent meals
Avoid eating within 3 hours of bedtime
Lose weight

**>**  
 Only about a third of patients with laryngopharyngeal reflux suffer from heartburn.

a number of possible causes (infection, environmental irritants, allergies, temperature/climate change, among others) are seen on endoscopic examination, with little correlation with symptom severity. In fact, 74% of otolaryngologists responding to a recent survey said they relied more on patient symptoms than on laryngeal signs for an LPRD diagnosis.<sup>10</sup>

■ **The Reflux Finding Score (RFS)**, available at [http://www.nature.com/gimo/contents/pt1/fig\\_tab/gimo46\\_T3.html](http://www.nature.com/gimo/contents/pt1/fig_tab/gimo46_T3.html), is a clinical tool developed to quantify laryngeal inflammation and standardize objective endoscopic findings. The RFS incorporates the following endolaryngeal signs:

- subglottic edema
- ventricular obliteration
- erythema/hyperemia
- vocal cord edema
- diffuse laryngeal edema
- posterior commissure hypertrophy
- granuloma/granulation tissue
- thick endolaryngeal mucus.

A numeric value is assigned to each, based on whether it is present or absent; partial or complete; local or diffuse; or mild or severe. However, the RFS, too, is an imperfect tool. Clinicians who have used the RFS report that a score higher than 7 identifies LPRD with 95% sensitivity.<sup>11</sup> But laryngeal findings may be due to other causes, such as infection, autoimmune reaction, or even allergies,

and studies have found the RFS to have poor specificity and inter-rater reliability.<sup>12-14</sup>

■ **Ambulatory dual probe pH monitoring** was considered to be the gold standard test for LPRD at one time, but newer studies have raised questions about its validity and usefulness, especially in patients taking proton-pump inhibitors (PPIs).<sup>1,5,7</sup> Newer advanced probes featuring less invasive data collection and greater sensitivity are under development. Ambulatory 24-hour multi-channel intraluminal impedance with pH monitoring is the most promising new diagnostic tool, as it can monitor both acidic and nonacidic reflux and distinguish between gas and liquid.<sup>15</sup>

**Treatment, like diagnosis, is not clear-cut**

LPRD is often called a diagnosis of exclusion, because of the nonspecific nature of its signs and symptoms and the importance of considering a range of other etiologies. The differential diagnosis includes excessive voice use, postnasal drip, upper respiratory infection, habitual throat clearing, allergic rhinitis, environmental irritants, temperature/climate change, chronic or episodic use of alcohol and/or tobacco, and psychological problems related to tics, such as habitual throat clearing or coughing.<sup>5</sup>

Diagnosis is often based on an empiric trial of high-dose PPIs, with confirmation dependent on symptom relief. Because there have been few placebo-controlled trials with PPIs and those that have been completed had conflicting results, diagnosis based on a combination of medical history and endoscopic laryngeal examination may be a better approach.<sup>16,17</sup>

■ **Acid suppression therapy** with either PPIs or histamine-2 (H2) receptor blockers such as ranitidine or famotidine is the mainstay of treatment for LPRD. But medical societies offer conflicting advice. The American Gastroenterological Association cautions clinicians not to prescribe acid-suppression therapy for patients with LPRD unless they also have GERD.<sup>6</sup> The American Academy of Otolaryngology-Head and Neck Surgery recommends twice-daily PPI use for

≥6 months.<sup>1,13</sup> The general consensus, based on clinical experience alone, is that patients should be treated with high doses of PPIs (eg, 40 mg omeprazole twice a day) for ≥6 months, with the addition of an H<sub>2</sub> receptor blocker to help reduce overnight acid production.<sup>1,18</sup> Prophylactic antacid use is also recommended in anticipation of reflux, such as before exercising and right after a meal.

Symptoms should start to improve within 6 to 8 weeks, and patients should be reassessed in about 3 months. To avoid a rebound effect from the abrupt cessation of medications, we suggest a gradual taper over 16 weeks. For the first 8 weeks, the H<sub>2</sub> blocker should be discontinued and the PPI decreased from twice a day to once. If symptoms are still controlled, the PPI dose can be reduced to once every other day for another 8 weeks, then stopped if symptoms do not recur.<sup>18</sup>

■ **Lifestyle and dietary changes** (TABLE 2), such as smoking cessation, weight loss, and avoidance of alcohol, are an important part of LPRD treatment, and may be used as a first-line therapy before prescribing medication.<sup>19</sup> In fact, some studies have found PPI therapy to be inferior to behavioral/lifestyle modifications.<sup>17</sup>

■ **Fundoplication surgery**, a procedure in which the gastric fundus of the stomach is wrapped around the lower end of the esophagus and stitched in place to prevent reflux, may be an option for patients who do not respond to, or cannot tolerate, aggressive medical treatment for LPRD. A 2006 prospective controlled study found that surgical fundoplication did not consistently relieve laryngeal symptoms.<sup>20</sup> But other studies have found that a carefully selected population with medically unresponsive laryngopharyngeal symptoms can benefit from this procedure.<sup>21,22</sup> One study showed a significant improvement within one month of fundoplication, with continued improvement observed during a 3-year follow-up.<sup>21</sup> In another prospective study, researchers showed that while LPRD-related laryngeal symptoms such as coughing and throat-clearing improved with both medical therapy and laparoscopic fundoplication, voice quality and endoscopic laryngeal/pharyngeal findings improved significantly only with the surgical procedure.<sup>23</sup>

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## CORRESPONDENCE

Shoib Sana, DO, Detroit Medical Center, Otolaryngology-Head and Neck Surgery, 6533 East Jefferson Avenue, Apartment 316, Detroit, MI 48207; ssana@dmc.org

➤ An empiric trial with high-dose proton-pump inhibitor therapy is a commonly used means of diagnosing LPRD, with confirmation based on symptom relief.

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