



## Laryngopharyngeal Reflux: What Do We Know?

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### Editorial

Laryngopharyngeal Reflux (LPR) is understood as a backflow of gastric contents (acid and pepsin) of liquid or aerosol to the supraesophageal organs. Synonyms for LPR are extraesophageal reflux, supraesophageal reflux, gastropharyngeal reflux, atypical reflux, silent reflux, laryngeal reflux and pharyngoesophageal reflux. Hereinafter the term laryngopharyngeal reflux will be used. This term was also used in the position paper of the committee on speech, voice and swallowing disorders of the American Academy of Otolaryngology - Head and Neck Surgery [1]. Unlike gastroesophageal reflux, LPR is not necessarily associated with the three guiding symptoms heartburn, acid reflux and regurgitation. LPR offers a variety of symptoms like throat clearing, mouth burning, globus, hoarseness, dysphagia, cough unknown genesis even in children, paroxysmal laryngospasm and dental erosions [1,2]. Each of the symptoms listed above can indeed point to an LPR but they are not specific to it. Every single symptom may have a different cause, e.g. infections, vocal overuse or misuse, allergies, smoking, inhalation of environmental irritants, alcohol abuse, drugs, tumors, psychosomatic disorders and others. Symptoms may be unreliable. Therefore and to objectify LPR a valid examination method with reproducible results is mandatory.

Gastroesophageal reflux (GERD) disease occurs mainly in supine position and LPR almost always in upright position [3,4]. LPR does not commonly appear in the context of food ingestion. In LPR the reflux is often an aerosol and not liquid as it is in GERD. This is a more plausible explanation of the presence of refluxate deep in the lungs [5,6]. There is strong evidence that LPR favors a number of other diseases such as asthma, obstructive sleep apnea, subglottic stenosis, chronic rhinosinusitis or otitis media with effusion in children [7-11]. Patients with the above mentioned symptoms represent approximately 10% of all patients presented in an ENT-clinic [1]. It is assumed that between about 50 and 80% of the patients with voice disorders also have laryngopharyngeal reflux [12,13]. The pathogenesis of reflux disease is complex. In LPR the primary disorder is often a disturbed function of the upper esophageal sphincter (UES) [14]. Up to 50 reflux episodes a day are considered normal for the esophagus. For the laryngeal mucosa, three reflux episodes are sufficient to induce inflammation and a significant disease [1]. In the esophagus pepsin can cause damage if the pH is less than 4, but in the supraesophageal regions like the laryngeal mucosa damage caused by pepsin can occur at higher pH. Chronic pepsin exposure as a result of LPR plays a significant role in laryngopharyngeal carcinogenesis [15]. Pepsin has a maximum activity at pH 2.0 and is inactive at pH 6.5 or higher, but it remains stable until pH 8.0 and can be reactivated when the pH is reduced [16]. Sandner "et al." [17] demonstrated that human gastric juice increased the number of DNA-stand breaks at pH 4.5 and 5.5 in epithelial cell cultures.

Really remarkable is, that refluxate always contains pepsin, even if devoid of acid (as might happen on high dose proton pump inhibitor (PPI) treatment), the enzyme will still be damaging if reflux reaches the extraesophageal areas [18]. Thus the LPR is not only a disorder which affects the quality of life, but can also become a serious disease. The diagnostic investigation of LPR is challenging. The medical history is not pointing the way. No matter how long the symptoms like hoarseness or others already existed or how stressful these have been felt by the patients, a correlation between the presence of LPR and symptoms could not be detected [4,19]. The duration and intensity of symptoms could not show a correlation with the presence of LPR. Some authors report about a correlation of laryngeal mucosal changes such as redness, edema of the arytenoids or a cobblestone appearance of the interarytenoid area and LPR. But laryngeal findings attributed to LPR can be found in 86% of normal controls [20]. These findings are not specific. The use of questionnaires does not lead to a valid diagnosis. There are two recommended questionnaires. The usefulness of these questionnaires is controversially discussed [21].

Until now it was impossible objectively to prove LPR. There are difficulties with traditional pH probes, they are positioned too low in the esophagus to detect LPR. The usual esophagus pH-probes

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must be rinsed with liquid all the time. If a proximal probe from beneath UES to above UES is re-positioned, it does not provide valid measurements anymore. The sensor will dry out due to air contact. Mucosal contact in the esophagus can mask reflux events. Esophageal pH testing using pH catheters, once considered the gold standard for diagnosing GERD, have not shown usable sensitivity and specificity for LPR patients [22]. Meanwhile, there is an oropharyngeal pH probe system for the evaluation of pH values in the region of interest. The restech Dx-pH-probe is inserted transnasally into the oropharynx behind the uvula. This is easily confirmed by visualization of the red LED on the tip of the catheter. At a frequency with two Hz the pH is measured. The transmission of the data is wireless to a recorder [22]. The patients wore the probes for 24 hours before removal.

The sensor detects aerosolized and liquid acid /alkaline and is specially developed for the pharynx. It does not require immersion in liquid. It is an easy minimal invasive application. In our experience patients show excellent acceptance of the pharyngeal probe. Measurement take place at the region of interest namely in the pharynx. Symptoms of laryngopharyngeal reflux are more prevalent in patients with esophageal adenocarcinoma (EAC) than typical GERD symptoms and may represent the only sign of disease [23]. So Reavis "et al." [23] figured out that the presence of LPR symptoms better identifies patients with existing cancer at an earlier stage than typical GERD symptoms. Just to remember the growing prevalence of EAC in the Western World, which shows the highest increase of 850 % since 1975 [24]. Unfortunately despite the immeasurable advantages of the pharyngeal 24-pH- monitoring there is no stated consensus in diagnosis of LPR. But this is not an uncommon phenomenon, when a new insight starts to clear things and correct previous accepted untested truths.

In different guidelines in different countries the empiric treatment with proton pump inhibitor as a diagnostic tool is still recommended. Empiric treatment with proton pump inhibitor is not without side effects [25]. For the diagnosis of LPR is it no help to identify non-responder to PPI. Empiric treatment can make healthy people sick. The unreflected medication with proton pump inhibitor may cause reflux in normal volunteers. Reimer "et al." [26] demonstrated in their study that proton pump inhibitor therapy for 8 weeks induces acid-related symptoms in healthy volunteers after withdrawal. Their results support the hypothesis Rebound Acid Hypersecretion (RAHS) has clinical consequences. Testing the therapeutic indication prior prescribing drugs for empiric trial saves money and provides a faster diagnosis and improved outcome. A definite diagnosis improves the adherence to the selected therapy. A negative result in the pharyngeal 24-pH- monitoring can exclude LPR as a cause of unspecific symptoms. Recently published studies indicate the benefit of this system as a tool in detecting LPR and its ability to predict responsiveness to medical and surgical therapy [27].

## Conclusion

Big advantage of the pharyngeal 24-pH-monitoring is the objective proof of LPR at the region of interest that medically non-indicated empirical drug treatments – e.g. with proton pump inhibitor – can be avoided and the patient thus be protected from their known side effects.

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