Impact of pH Monitoring on Laryngopharyngeal Reflux Treatment: Improved Compliance and Symptom Resolution


OBJECTIVES Treatment of laryngopharyngeal reflux (LPR) often suffers from poor patient compliance and hence poor symptom improvement. The aim of this study was to determine whether 24-hour oropharyngeal pH monitoring was associated with higher rates of treatment compliance and symptom improvement compared with empirical treatment for LPR.

STUDY DESIGN Retrospective, case-control study. In a tertiary care center.

SUBJECTS and METHODS Charts were reviewed from 170 consecutive adult patients diagnosed with LPR from January 2008 to March 2010. After clinical diagnosis, all patients were offered the option of empiric treatment with a proton pump inhibitor versus treatment based on a 24-hour oropharyngeal pH study using the Dx-pH system (Restech, San Diego, California). Treatment compliance and pretreatment and post treatment reflux symptom index (RSI) scores were compared for the 2 groups. Only consecutive patients with complete data were included.

RESULTS One-hundred and seventy patients were included in 2 groups. Group I consisted of 73 patients who underwent pH monitoring. Group II consisted of 70 patients treated empirically. Compliance with medication therapy (68.5% vs 50.0%, P = .019) and lifestyle modification (82.2 vs 25.7%, P = .0001) were greater among patients in group I. Symptom improvement was greater among patients in group I following treatment compared with patients in group II, with a significantly greater reduction in RSI (36.6% vs 24.4%, P = .023).

CONCLUSION Among our patient population, treatment of LPR based on pH monitoring resulted in greater compliance, as well as greater symptom improvement, compared with empirical therapy alone.

The Value of Routine pH Monitoring in the Diagnosis and Treatment of Laryngopharyngeal Reflux


OBJECTIVE To assess the need for pH testing in diagnosing laryngopharyngeal reflux (LPR). Study Design. Case series with planned data collection.

SETTING Tertiary care center. Subjects and Methods. On the basis of symptoms and/or abnormal endoscopic findings, more than 500 patients underwent 24-hour pharyngeal pH testing at a single center (using the Dx-pH probe) between January 2009 and June 2011. A total of 163 patients not on proton-pump inhibitors at the time of study and with complete data available for analysis (pH results, body mass index, smoking status, pretest reflux symptom index) were divided into 2 groups by positive (n = 70) and negative (n = 93) RYAN Score. The Reflux Symptom Index (RSI) was compared between groups and assessed overall against RYAN Score parameters at different pH thresholds. The diagnostic utility of an RSI ≥ 13 for prediction of RYAN Score was assessed.

RESULTS No significant difference in RSI was seen between RYAN-positive (17.50 ± 11.47) and RYAN-negative (14.95 ± 11.43) patients (P = .161). Overall, RSI correlated poorly with percentage time spent below pH thresholds 6.5, 6.0, 5.5, and 5.0 and upright and supine RYAN parameters at these thresholds (as determined by linear regression analysis). The sensitivity, specificity, positive predictive value, and negative predictive value of RSI ≥ 13 for RYAN positivity were 55.7%, 47.3%, 44.3%, and 58.7%, respectively.

CONCLUSION Our findings show that in our population of otolaryngology patients, the diagnosis of LPR cannot be reliably made on the basis of symptoms alone. Diagnosis, and in particular treatment decisions, should ideally be made on the basis of a combination of symptoms, signs, and confirmatory testing.

Esophageal motility abnormalities in patients with laryngo-pharyngeal symptoms: preliminary reports from a study conducted with high-resolution manometry and oropharyngeal pH monitoring

Vailati C, Mazzoleni G, Bondi S, Passaretti S, Bussi M, Testoni PA

INTRODUCTION Respiratory and laryngeal symptoms can occur both in patients with typical symptoms of gastroesophageal reflux disease (GERD) and in patients without typical GERD symptoms; mechanisms involved are both direct (aspiration) and indirect (neurally mediated). However, it is not known if patients with laryngopharyngeal symptoms (LPS) present specific esophageal motility abnormalities, especially in the upper esophagus.

AIM To evaluate the relationship between pathological oropharyngeal pH-monitoring and esophageal motor abnormalities in patients with GERD-related laryngeal
symptoms, assessed with high resolution manometry (HRM) and oropharyngeal pH-monitoring (Restech® probe).

**MATERIAL AND METHODS** 15 consecutive patients with chronic (> 6 months) LPS were prospectively enrolled from May to July 2011. A previous allergological and ear-nose-and-throat evaluation excluded other than GERD diagnosis. Reflux symptom index (RSI) score was recorded and only patients with a score > 13 were considered eligible for the study. A solid state with 36 transducers HRM was performed before the pH probe positioning; lower esophageal sphincter (LES) pressure, integrated relaxation pressure 4 sec (IRP-4s), upper esophageal sphincter pressure (UES), number of 5-ml wet swallows with a large transition zone (TZ) and motility characteristics (% peristaltic waves, distal contractile integral - DCI), of esophageal contraction were all recorded. Tracings were classified according to the Chicago Classification (Kahrilas PJ et al, J Clin Gastroenterol 2008). A ≥2 cm defect in the 30mm Hg isobaric contour at the level of the TZ was considered abnormal and defined as large TZ. 24-h oropharyngeal pH-monitoring, as described by Ayazi S - J Gastrointest Surg 2009, was performed after having stopped antisecretory therapy for at least 14 days.

**RESULTS** 8 patients (53.3%) had a pathological oropharyngeal pH-monitoring study and 7 patients (46.7%) had a normal oropharyngeal acid exposure. These groups were comparable regarding to demographic aspects. Manometric findings in the two groups are presented in table 1, as well as the p-value. Values are presented as mean ± standard deviation. The only statistical significant manometric finding was the number of peristaltic contractions with a large TZ, that resulted higher in patients with pathological oropharyngeal acid exposure.

**CONCLUSIONS** Patients with LPS and a positive Restech® study showed a higher percentage of peristaltic contractions with a large TZ compared to patients with normal Restech® study. Future and larger studies will have to demonstrate if this finding is just an epiphenomenon induced by GERD or it is involved in the onset of symptoms.

Pharyngeal pH Monitoring May Be Superior to Proximal pH Monitoring in the Detection of Laryngopharyngeal Reflux

Gastroenterology Vol. 140, Issue 5, Suppl 1, Page S-1035

**BACKGROUND** Determining a causal relationship between abnormal reflux into the proximal esophagus/pharynx and extraesophageal manifestations of gastroesophageal reflux disease (GERD) remains a diagnostic challenge. In this study we aim to determine whether pharyngeal pH monitoring provides superior sensitivity over dual-channel pH testing in detecting laryngopharyngeal reflux (LPR).

**METHODS** 7 control subjects and 17 symptomatic patients, 4 with typical GERD and 13 with primary respiratory symptoms, underwent 24-hour ambulatory esophageal multichannel intraluminal impedance (MII)-dual pH simultaneously with pharyngeal pH monitoring. The distal pH sensor was placed 5cm above the manometrically determined upper border of the lower esophageal sphincter (LES) and the proximal 15cm above. Pharyngeal pH was monitored concomitantly using a separate pH probe positioned 1 cm below the uvula. Data collection was synchronized between the devices. Esophageal reflux was considered present if pH dropped to <4 in either pH sensor, and/or a drop occurred ≥50% from baseline in impedance 3, 5, 7 or 9cm above LES (distal) or 15 and 17cm above LES (proximal). Separate pH thresholds of <5.5, 5.0, 4.5 and 4.0 were defined for reflux episodes detected in the pharyngeal probe.

**RESULTS** At a threshold of pH<5.5, an average of 1±4 pharyngeal reflux event over 24 hours was seen in control subjects. Symptomatic patients had greater pharyngeal pH exposure than controls, averaging 7±14 episodes/24 hours in those with typical GERD symptoms and 46±76 in those with respiratory symptoms. Total pharyngeal reflux events (603) were markedly more common in patients with respiratory symptoms than either control (10) or typical GERD symptoms (28). Further, the highest number of pharyngeal reflux episodes recorded across all pH thresholds was observed in subjects presenting with primary respiratory symptoms: 603, 91, 38 and 40 events at pH<5.5, 5.0, 4.5 and 4.0, respectively. 6 of the 11 patients with abnormal distal pH results had corresponding abnormal pharyngeal acid exposure; however, only 3 had concomitant positive proximal esophageal pH results. Pharyngeal pH also appears superior to the proximal esophageal pH in differentiating GERD related respiratory symptoms, as compared to gastrointestinal. Fundoplication normalized pharyngeal pH and markedly relieved symptoms in a single patient with severe respiratory symptoms and normal proximal esophageal acid exposure.

**CONCLUSIONS** The more common prevalence of pharyngeal reflux, as compared to proximal esophageal reflux, particularly in subjects with extraesophageal symptoms, suggests that pharyngeal pH monitoring may be a more sensitive diagnostic tool for LPR than proximal pH monitoring. Symptom relief and pharyngeal pH normalization post fundoplication provides further evidence of the utility of ambulatory pharyngeal pH monitoring.
Clinical utility of pharyngeal pH monitoring for hoarseness


OBJECTIVES To evaluate the contribution of 24-hour pharyngeal pH monitoring for the patient presenting with symptoms of hoarseness, globus, throat clearing, and sore throat.

METHODS Results of 167 pharyngeal pH studies performed for complaints of hoarseness, globus, and throat clearing at the Texas Center for Voice and Swallowing from 5/09–12/09 were analyzed for pharyngeal reflux pattern and severity. Patient records were reviewed for chief complaint, symptom duration, ten-item voice handicap index (VHI-10) and reflux symptom index (RSI) scores. MANOVA was used to compare symptom duration, VHI-10 scores, and RSI scores between those patients with and without abnormal pharyngeal pH studies.

RESULTS 72 studies (43%) were normal with zero events below pH 5.5. 59 studies (35%), or 60% of all positive studies showed nocturnal pharyngeal reflux only. 34 studies (20%) showed combination upright daytime reflux events and nocturnal reflux. Five studies (2%) had only upright events. There was no significant difference in presenting symptoms, symptom duration, or severity scores in the patients that had negative vs. positive pharyngeal pH studies.

CONCLUSIONS 24-hour pharyngeal pH study eliminates the diagnosis of reflux in a significant percentage of patients with hoarseness. Severity or duration of symptoms of hoarseness, globus, or throat clearing do not reliably predict presence of reflux.

Dx-pH monitoring: How does it compare to the standard pH probe?


PURPOSE Physiologic assessment of esophageal acid exposure is often performed utilizing ambulatory pH monitoring. Recently ambulatory Restech Dx-pH probe is designed to record pH changes in the oropharynx in patients with suspected extraesophageal reflux symptoms. However, there are no validations of this instrument against the current standards in clinical practice. Thus, we aimed to compare the internal consistency of the new distal esophageal Dx-pH probe with the standard of care Sandhill pH probe.

### METHODS

Patients diagnosed with GERD (esophagitis at endoscopy or prior abnormal pH findings of acid suppressive therapy) underwent simultaneous ambulatory esophageal pH monitoring. The Dx-pH and Sandhill pH probes were positioned at 5 cm above the manometrically measured LES in each patient. Based on the inherent property of the devices, Dx-pH monitor recorded esophageal acid exposure every 0.5 seconds compared to a 5 second interval for the Sandhill probes. Outcomes assessed included episodes below pH 6, pH 5, and pH 4 and % time below pH 4, 5, and 6. The # times that pH fell below the cutoff was manually and electronically measured. The values were compared using the Wilcoxon signed rank test on the differences in the paired data.

### RESULTS

A total of 11 patients (5 male and 6 female) with mean (range) age of 40.9 (21–59) constituted the study population. 72.7% and 45.4% of the patients were complaining of daily heartburn and regurgitation, respectively. No statistically significant \((P < 0.05)\) differences were found between the Dx-pH and Sandhill devices for the number of times \(\text{pH} < 4, \text{pH} < 5, \text{or} \text{pH} < 6\). The Dx-pH probe spent consistently more time at \(\text{pH} < 4 (P = 0.131), \text{pH} < 5 (P = 0.049), \text{and} \text{pH} < 6 (P =0.01)\) than the Sandhill probe.

### CONCLUSION

Dx-pH probe identifies reflux events in the distal esophagus similar to current standard pH catheter but it has less variability. The clinical potential of this diagnostic device will need to be tested in patients with extraesophageal GERD.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Restech (25-75%)</th>
<th>Sandhill (25-75%)</th>
<th>P Value</th>
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<tr>
<td># Events (\text{pH} &lt; 4)</td>
<td>37 (20-53)</td>
<td>34 (17-60)</td>
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<td>6.0 (1-10)</td>
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<td># Events (\text{pH} &lt; 5)</td>
<td>40 (18-55)</td>
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<td>% Times (\text{pH} &lt; 5)</td>
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<td>13.0 (1-24)</td>
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<tr>
<td># Events (\text{pH} &lt; 6)</td>
<td>36 (9-62)</td>
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<td>% Times (\text{pH} &lt; 6)</td>
<td>43.0 (12-56)</td>
<td>23.0 (6-45)</td>
<td>0.01</td>
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</tbody>
</table>
First Agreement Analysis and Day-to-Day Comparison of Pharyngeal pH Monitoring with pH/Impedance Monitoring in Patients with Suspected Laryngopharyngeal Reflux

J Gastrointest Surg 2012 Mar 27. [Epub ahead of print]

OBJECTIVE Diagnosis of laryngopharyngeal reflux (LPR) is still challenging. Recently a diagnostic device for pH values in the aerosolized environment of the pharynx has been introduced (Dx-pH). We evaluated results of Dx-pH with objective criteria of pH/impedance monitoring (MII) and subjective reflux scoring systems and assessed day-to-day variability.

DESIGN This study makes use of a prospective single-center trial. Thirty patients with suspected LPR were analyzed. Upper endoscopic examination, manometry, phoniatric examination, and reflux scores were assessed. Dx-pH was performed on two consecutive days, first in combination with MII and second as single measurement. Thereafter, proton pump inhibitor (PPI) trial was performed. Patients were interviewed about symptom relief after 3 months.

RESULTS There were considerable differences between MII and results on Dx-pH: day 1 (agreement 11 out of 30, kappa 0.137) and day 2 (agreement 14 out of 30, kappa 0.036). Statistically significant differences were detected correlating all single reflux episodes (n=453) of Dx-pH with MII and vice versa. Furthermore acidic reflux episodes did not result in pH drops of the pharynx. There was a fair agreement between Dx-pH measurements on subsequent days. After follow-up, 3 out of 18 patients with pathological Dx-pH results reported positive response to PPIs, in contrast to 5 out of 6 patients with pathological MII.

CONCLUSION According to our data, acid pharyngeal pH levels detected with Dx-pH are not related to GERD and acid esophageal reflux episodes do not result in pharyngeal pH alterations. Hence, present etiology of LPR needs to be reconsidered since neither mixed nor gas reflux events result in pharyngeal pH alteration. Other acid-producing or retaining factors should be taken into account.

Oropharyngeal pH-monitoring with the Restech probe for laryngo-pharyngeal reflux: A new reliable test before PPI therapy?


INTRODUCTION Respiratory and laryngeal symptoms can occur both in patients with typical symptoms of gastro-esophageal reflux disease (GERD) and in patients without typical GERD symptoms; in this setting, there are no specific clinical or pathological findings to identify reflux as the cause of the laryngo-pharyngeal symptoms (LPS) and current methods of measuring pharyngeal pH environment are inaccurate and problematic due to artifacts. The Restech® oropharyngeal probe may overcome these limitations.

AIM To evaluate the relationship between pathological oropharyngeal pH-monitoring and clinical response to a 3-month double dose PPI therapy in patients with GERD-related laryngeal symptoms.

MATERIAL AND METHODS 18 consecutive patients with chronic (> 6 months) LPS were prospectively enrolled from May to July 2011. A previous allergological and ear-nose-and-throat evaluation excluded other than GERD diagnosis. Reflux symptom index (RSI) score was recorded and only patients with a score > 13 were considered eligible for the study. 24-h oropharyngeal pH-monitoring, as described by Ayazi S - J Gastrointest Surg 2009, was performed after having stopped antisecretory therapy for at least 14 days. All the patients were given a 3 months therapy with pantoprazole 40 mg bid and then repeated the RSI score. Patients were considered as responders if a 5-point decrease in RSI score was recorded.

RESULTS 13 patients (72.2%) were considered responders; 9 patients (50.0%) had a pathological oropharyngeal pH-monitoring study. Groups of responder and non responder patients were comparable regarding to demographic aspects. All the patients with a positive Restech® study were responsive to PPI, and 5 out of 9 patients with a negative Restech® study were non responders, with this difference being statistically significant (p=0.03). Responder patients resulted also in a higher rate of oropharyngeal acid exposure, expressed as Ryan Score, both in orthostatic and in supine position, compared to non responders (49.74 and 9.64 vs 2.12 and 2.17, p<0.05). Mean RSI score before therapy was 16.6±3.1. Considering non responder patients, RSI score dropped from 16.25±3.9 to 7.87±3.2 after PPI therapy (p<0.05), whereas a not statistically significant reduction was observed in non responder patients (17±3.2 to 10.4±3, p=0.13).

CONCLUSIONS All patients with pathological oropharyngeal acid exposure assessed with the Restech® probe clinically responded to a 3 months course of double dose PPI therapy. In the light of these results, if confirmed by future larger studies, the Restech® evaluation could be proposed as a tool for a better stratification of patients with LPS before starting a long medical therapy, which is generally associated with low rates of treatment compliance.
Detecting reflux in adults with Eustachian tube dysfunction


OBJECTIVE 1) Ascertain whether adult patients with Eustachian tube dysfunction (ETD) have a higher incidence of reflux into the nasopharynx compared with controls. 2) Utilize recent advances in pH probe technology to detect acidity at the Eustachian tube orifice for direct comparison.

METHODS A prospective study was performed on 38 adult patients in an outpatient setting between November 2009 and February 2011. Seventeen patients with Eustachian tube dysfunction and 21 control subjects had a Dx-pH probe (Restech, San Diego, California 2006) placed near the torus tubarius in the posterior nasopharynx for 24 hours.

RESULTS The average pH value obtained from the nasopharynx of adults with no history of ETD was 7.03 (range, 6.10-7.92; SD, 0.69). In comparison, the average pH for patients with ETD was 6.90 (range, 5.33-8.06; SD, 0.77). This P value for this difference was 0.48. The average number of reflux events for subjects was 0.55 events over a 24-hour period for controls and 2.1 for patients with ETD. Decreases in pH were considered reflux events if the pH dropped below 5.5 while in the upright position or below 5.0 in the supine position.

CONCLUSION By utilizing a novel pH probe that allows detection of acidity in a non-liquid environment, a comparison of nasopharyngeal pH between control patients and those with ETD was performed. A trend toward higher numbers of reflux events was found in patients with ETD when compared to control subjects.

Treatment of extraesophageal reflux with nasal CPAP in patients with obstructive sleep apnea


INTRODUCTION Nocturnal gastroesophageal reflux disease (GERD) resulting in extraesophageal reflux (EER) may contribute to airway inflammation and worsen obstructive sleep apnea (OSA). Conversely, OSA may aggravate nocturnal EER. We hypothesize that patients with OSA and GERD are at an increased risk for nocturnal EER and that continuous positive airway pressure (CPAP) will lead to its reduction.

METHODS Consecutive patients with GERD were enrolled if they required a polysomnography (PSG) for suspected OSA. All patients were tested off acid-suppressive medications. Each patient completed a 2-day diagnostic and therapeutic PSG with continuous monitoring of aerosolized pH by a probe placed into the posterior oropharynx through the nares. Wilcoxon signed-rank test was used to analyze paired data on the rate of EER before and after CPAP. Kendall’s Tau coefficient was calculated to determine whether any improvement in the EER as a result of CPAP correlated with the baseline severity of EER.

RESULTS 8 subjects were enrolled. All were confirmed to have OSA with a median apneahypopnea index (AHI) of 54, improving to 6 on CPAP (p=0.008). The severity of EER at baseline was variable with a median reflux rate of 6 (IQR 3.5–23). We observed a non-significant reduction in the EER rate following CPAP (median: 0.8 vs. 0.4 events/hour, p=0.22) in the overall comparison. However, when accounting for the severity of the underlying EER, a statistically significant reduction in EER following CPAP was observed for those with more severe EER at baseline (Tau=0.71, p=0.013).

CONCLUSION CPAP may be effective in improving moderate to severe nocturnal EER. Its efficacy however is dependent on the severity of the underlying EER. Further prospective study is in need.

Gastroesophageal reflux (GER) presenting with obstructive sleep apnea syndrome – Arousal-related activity in excessive daytime sleepiness (EDS)


BACKGROUND/OBJECTIVE The excessive daytime sleepiness (EDS) with snoring is a core symptom of obstructive sleep apnea syndrome (OSAS). There is however, only a low correlation between the severity of the OSAS and EDS. Resulting from symptomatic GER compounded by arousals, poor sleep quality (s. Lit. 1). EDS, snoring and GER are positively correlated (s. Lit. 2). Asymptomatic GER leads to arousals with insomnia (s. Lit. 3). Can possibly the increased arousal activity explained by the different GER characterizes her EDS in OSAS?

METHODS/PATIENTS 11 patients (10 men, 1 woman, mean age 46 J (23-74), BMI m 29 (25-39) for the investigation of SRBD after previous outpatient testing were introduced to the SL Stationary PSG (Alice-V system, Heinen & Loewenstein) evaluated manually AASM with simultaneous and time synchronous oropharyngeal pH monitoring (Laryngopharyngeal Reflux Measurement, Restech Dx-pH, pH <6, > 5', > 5% ↓).

Outpatient Sleep Center Sleep vigilance parameter:
- Epworth Sleepiness Scale (ESS): > 8
- Pupillographic sleepiness test (PST): Pathologic
Vigilance Quaternary-Maly 30 minutes: PR <32
Exclusion Criteria: Symptomatic GER; Taking PPIs; Poor cooperation; Intolerance of the LPR probe.

CONCLUSION LPR is a frequent event in saturated OSAS. The monopolar method esophageal endoscopy the 2-channel technology superior (s.Abb.3). Reflux events generate a high number of arousals. The CAP-arousals are obvious characteristic of reflux dependence (S.Lit.4). The lengths of reflux episodes leading to arousals lead differ greatly. Short pH events do not lead conclusively to an arousal. At EDS, with only mild obstructive sleep apnea syndrome (UARS) is to note the form of arousal. A negative reflux history with CAP-arousals which pH monitoring is indicated. In addition to the CPAP therapy discussion of aggressive use of PPI.

Gastroesophageal reflux disease in bronchial asthma: A preliminary report from a developing country

Onyekwere C, Adeye C, Ogbere A.
Canadian Association of Gastroenterology. 2010

AIMS 1) To determine the prevalence of symptomatic GERD among a population of known bronchial asthma patients and non asthmatic control matched for age and sex. 2) To document endoscopic findings in the patients found to have GERD and compare asthma severity in those asthmatics with and without GERD. 3) To determine GERD prevalence in the study subjects with and without obesity.

METHODS The subjects were diagnosed Asthmatics attending clinic at a University teaching hospital. Consecutive asthmatics were enrolled into the study after due consent. The control subjects were non-asthmatics and consisted of hospital workers. They were randomly recruited to match the asthmatics for age and sex. Ethical approval was obtained before commencement of the study in September 2007. An interviewer administered validated GERD questionnaire (F-scale) 1 was used. Subjects’ biodata, anthropometric indices as well as their pulmonary function results were documented. Patients found to have GERD (F-scale score> 7) were invited to undergo a 24 hour PH study using a new Oropharyngeal PH probe (RESTECH) as well as an upper gastrointestinal endoscopy examination. All data were collated and analysed using Microsoft SPSS software package.

RESULTS Ninety-eight Asthmatics (mean age (SD) 39.8 years (17) and male: female ratio of 1:1.5), and 78 control (mean age (SD) 34 years (12) and M: F ratio of 1:1.8) were studied. 16 (16%) Asthmatics and 11 (16%) controls had a BMI> 30. The prevalence of symptomatic GERD in asthmatics and controls was (42%) and (35%) respectively; the difference was significant (chi square 52.68, p<0.01). Among the asthmatics 69 had abnormal PEFR while it was normal in 15. Of those with abnormal PEFR, 27 (39%) had F scale > 7 while in remaining 42 (61%) F scale was less than 7. The duration of asthma diagnosis ranged from 1month to 40 years; mean (SD) 7.8years (10). The asthma duration was short (<5years) in 43, medium (<10 years) in 12, and long duration (>10) in 39. F scale > 7 was noted in 13 (30%) with short duration, 6 (50%) medium duration, and 22 (56%) long duration of asthma diagnosis. 10 (37%) of obese subjects (BMI>30) had F-scale >7 while 28 (35%) of non-obese subjects had F scale > 7. The difference was significant (chi square 203, p<0.001.)

CONCLUSIONS The study has shown a significant higher prevalence of symptomatic GERD among asthmatics than a control with obese patients having a higher prevalence than non-obese. Among asthmatics, GERD prevalence appears to be related to the duration of asthma rather than severity as measured by PEFR. The symptom survey are corroborated by endoscopic as well as PH assessment. Further studies on the mechanisms underlying GERD in asthma as well as trial of antisecretory drugs in asthmatics are required.

The effect of singing on laryngopharyngeal reflux

Fink D, Bhatnagar S, Song P, Bunting G.
Otolaryngology -- Head and Neck Surgery 2011 145: P83

OBJECTIVE While there has been widespread conjecture regarding the role of laryngopharyngeal reflux in singing, there remains no objective data demonstrating that voice use causes increased reflux. We attempted to objectively analyze pharyngeal pH changes during singing to better understand how it is affected by singing.

METHODS Eight singers underwent 24-hour pharyngeal pH probe testing with the Restech Dx-pH Measurement SystemTM, one hour of which was spent singing. The mean pH and number of pH drops were recorded. A one-tailed t test was used to compare the mean pH of the time singing with the 2 control values.

RESULTS The mean pH for the control time was 6.8347, for the control time without the time supine was 6.9164, and for the time singing was 7.0286. We were thus able to reject the null hypothesis that singing decreases laryngeal pH (P = .035). There was an increase in mean pH during the time singing as compared with the 2 control groups.

CONCLUSION While singers may have increased reflux complaints, our data suggest that the singing itself does not cause an increase in acid exposure to the laryngopharynx.
Does laryngopharyngeal reflux cause intraoral burning sensations? A preliminary study

Becker S, Schmidt C, Berghaus A, Tschiechner U, Olzowy B, Reichel O.
Eur Arch Otorhinolaryngol. 2011 Sep;268(9):1375-81.

BACKGROUND Intraoral burning sensations are a common problem in the otolaryngological practice.
AIM The aim of this study was to evaluate if laryngopharyngeal reflux can cause intraoral burning sensations by measuring oropharyngeal acid reflux. Patients with recurring intraoral burning sensations underwent oropharyngeal pH monitoring in our outpatient clinic. The pH catheter was placed at the level of the uvula. The catheter contained an externally worn transmitter, which wirelessly sent the data to a monitor. In addition, patients were instructed to indicate meals or the occurrence of burning sensations by pressing provided buttons on the monitor. Corresponding events of burning sensations and a significant decrease in oropharyngeal pH values should be visualized.
RESULTS Twenty-two patients suffering from recurring intraoral burning sensations underwent oropharyngeal pH measurement for 21-25 h. We could find oropharyngeal reflux episodes in 11 patients. However, we could not detect any episodes of burning sensations in the mouth corresponding with a decrease in oropharyngeal pH values.
CONCLUSIONS Our results suggest that there is no causal connection between LPR episodes and the occurrence of intraoral burning sensations in the examined patients. Although further studies with more patients are necessary in the future, we conclude from our findings that recurring intraoral burning sensations are not an indication for proton pump inhibitor therapy.

Reflux in head and neck cancer patients after chemoradiation

Cho A, Lewis E, Nathan C.
American Head and Neck Society - Annual Meeting, P054. 2010

OBJECTIVES To determine if reflux is increased in laryngohypopharyngeal cancer patients who have had radiation (XRT) ± chemotherapy compared to non-radiated patients.
DESIGN Prospective study at a State University Hospital
PATIENTS Twelve patients with advanced head and neck cancer were evaluated for reflux events using a nasopharyngeal 24 hour pH probe in the last year. Three patients had XRT ± chemotherapy as primary treatment and nine patients were newly diagnosed and treatment was not yet initiated before the pH probe reflux study was performed. There were no patients on reflux medications at the time of the pH probe study except one patient who still had considerable reflux despite the medication.
MEASURES RYAN scores measuring positive reflux events.
RESULTS The majority of patients had laryngeal cancer (83%). All patients who were treated with XRT ± chemotherapy primarily had significant reflux as indicated by considerably higher RYAN scores (mean of 547.42 ± 303.59 upright) compared to those who did not have XRT ± chemotherapy (mean of 37.42 ± 63.70 upright) (p=0.0004). Two of the three patients treated primarily with XRT ± chemotherapy had reflux in upright and supine positions, while one patient only had reflux in the upright position. Four of the nine non-radiated patients had reflux only in the upright position, and no one had reflux in the supine position. The mean supine RYAN scores of patients treated with XRT ± chemotherapy was 27.88 ± 35.41 compared to 2.88 ± 1.23 in non-radiated patients (p=0.0398).
CONCLUSIONS This preliminary study demonstrated that XRT ± chemotherapy caused significant increase in RYAN reflux score compared to non-radiated patients. Given that XRT causes xerostomia and the absence of the neutralizing affect of bicarbonate in the saliva, we believe that XRT causes a significant increase in LPR. Although this is a pilot study and the numbers are still small, the results are striking and there is no objective data in literature linking XRT to reflux at this time.

The role of poor oesophageal clearance in patients with suspected laryngopharyngeal reflux

Tan K, Raeburn A, Emmanuel A.

INTRODUCTION Laryngopharyngeal reflux (LPR) disease is thought to occur in one-third of gastro-oesophageal reflux disease (GORD) patients. Currently there is no gold standard investigation for patients with suspected LPR. The Restech Dx-pH measurement system is reported to be capable of detecting liquid or aerosolized acid reflux in the upper airway, and may be valid objectifiable measure of LPR. We postulated that elevated Restech Dx-pH results may be related to poor oesophageal clearance of acid.
METHODS Thirty-eight consecutive patients referred for investigations of LPR underwent standard stationary oesophageal manometry and ambulatory dual channel pHmetry with sensors 5cm and 20cm above the lower oesophageal sphincter. The Restech Dx-pH sensor was placed in the oropharynx transnasally. The RYAN composite score was generated by analysis software and was used to determine test outcome. Patients were stratified into two
groups based on the total percentage time of pH<4 detected in the distal channel of pHmetry. Group A had a total percentage of time more than 4.5% and Group B less than 4.5%.

RESULTS Five patients were excluded in the analysis due to technical or equipment errors. In Group A (n=16), 50% of the patients had positive Ryan score. The average age of these patients with positive Ryan score was significant higher (58± 12.5 vs 43 ± 12/7 years, p=0.0389) compared to patients with negative Ryan score. The mid oesophageal contraction amplitude was significantly higher in Group A (47 ± 25.9 vs 22 ±8.1 mmHg, p=0.04894). The LOS pressure was significantly lower in patients with positive than negative Ryan score in Group B (9 ± 2.6 vs 14 ± 3.9 mmHg, p=0.01347).

CONCLUSION In this tertiary-referred population with LPR symptoms, almost 50% had significant acidification in the upper airway possibly explaining their symptoms. Poor oesophageal clearance of refluxed acid, reflected in reduced contraction amplitude in the oesophageal body may also play a role. Interestingly, patients with normal distal acidification who have high levels of pharyngeal acid exposure tend to have lower LOS pressure and poor body motility.

Identifying the causes of reflux events and symptoms - New approaches

Fox M.
Aliment Pharmacol Ther 2011.

Gastro-oesophageal reflux disease (GERD) is present if the passage of gastric contents back into the oesophagus causes either mucosal disease or symptoms. The aim of clinical investigation in patients with suspected GERD is not only to establish the diagnosis, but also to identify underlying pathology and guide specific management. Unfortunately, standard endoscopy and physiological measurement of oesophageal function by manometry and ambulatory pH measurement rarely meet these ideals. The need to improve clinical management of patients, especially those with endoscopy negative disease and symptoms persisting during acid-suppressive therapy has refocused attention on the pathophysiology of disease. This review summarises new approaches and new technologies that have been introduced for the investigation of GERD. These include high-resolution endoscopy, detection of dilated intercellular spaces on histology, combined pH impedance studies, prolonged wireless pH monitoring, detection of aerosolized acid in the pharynx, detection of peptic in expectorated saliva, measurement of gastro-oesophageal distensibility and monitoring of gastro-oesophageal function after a meal by high resolution manometry. The potential role of these advances to improve clinical practice is considered. Throughout, emphasis is given to the need to identify underlying causes of reflux events and symptoms and how the findings of investigation could be used to guide rational and effective treatment.

Reflux revisited: Advancing the role of peptic
Bardhan K, Strugl V, Dettmar P.

Gastroesophageal reflux disease is mediated principally by acid. Today, we recognize reflux reaches beyond the esophagus, where peptic, not acid, causes damage. Extraesophageal reflux occurs both as liquid and probably aerosol, the latter with a further reach. Pepsin is stable up to pH 7 and regains activity after reacidification. The enzyme adheres to laryngeal cells, depletes its defenses, and causes further damage internally after its endocytosis. Extraesophageal reflux can today be detected by recognizing pharyngeal acidification using a miniaturized pH probe and by the identification of peptic in saliva and in exhaled breath condensate by a rapid, sensitive, and specific immunoassay. Proton pump inhibitors do not help the majority with extraesophageal reflux but specifically formulated alginates, which sieve peptic, give benefit. These new insights may lead to the development of novel drugs that dramatically reduce pepsinogen secretion, block the effects of adherent peptic, and give corresponding clinical benefit.

Oropharyngeal pH evaluation to determine the presence of airway reflux in asthmatic patients

Jackson WR, Burke J, Morice A.
European Respiratory Society Congress, 2011.

INTRODUCTION Reflux disease can affect the tracheobronchial tree directly, this has been shown to lead to aspiration, until recently pharyngeal pH measuring detects only liquid reflux. A new pharyngeal probe which detects not only liquid acid but more importantly aerosolized acid has been shown to overcome the artifacts that occur in measuring pharyngeal pH with existing oesophageal catheters and it is now commercially available to measure LPR. It is the ‘Restech Dxp-pH measurement system’ (Respiratory Technology Corporation, San Diego, California, USA). Prior to the introduction of this system, identifying gastroesophageal reflux as a potential origin of certain respiratory complaints using an accurate, real-time measurement of airway pH was not possible.

PURPOSE To evaluate the presence of gaseous airway reflux in physician diagnosed asthmatic patients, utilizing
the ‘Dx-pH Measurement System’. The Dx-pH probe can detect the pH of aerosolized droplets and liquid.

METHODS Asthmatic patients with symptoms assessed on the Hull Airway Reflux Questionnaire (HARQ) underwent 24-hour airway pH monitoring with the Dx-pH measurement system. The probe was inserted trans-nasally into the oropharynx with the distal end sitting lateral to the uvula. A RYAN score (composite pH score for pharyngeal acid exposure) was calculated for both the upright and supine periods. In the upright period, 5.5 is the best pH threshold to define abnormal acid exposure, while pharyngeal acid exposure is considerably higher in the supine period and a lower threshold is necessary. For the supine period, pH <5.0 maximizes sensitivity and pH < 4.5 maximizes specificity. The ‘RYAN Score’ was developed and has been incorporated into Restech’s pH data analysis software. The values obtained can now be used to determine if patients with laryngeal or respiratory symptoms have abnormal pharyngeal acid exposure.

RESULTS The study population consisted of 12 asthmatic patients (1 male, 11 female) with a mean age of 50 (range 33-72). RYAN score values for the upright period were 2.12-612.57 (normal <9.41) and for the supine period were 2.17-38.01 (normal <6.80). The mean Hull Airway Reflux Questionnaire score was 32/70 (normal <13). Airway reflux was present, confirmed by an abnormal RYAN score in 75% of the study population in the upright position and 58% in the supine position.

CONCLUSION Airway reflux is a frequent condition in asthma patients. It should be recognized as a distinct entity that warrants specialized focus and treatment to improve the symptoms of patients suffering with extraesophageal reflux and asthma. The Dx-pH probe is a useful diagnostic tool for patients with asthma and symptoms suggestive of airway reflux.

Extraesophageal reflux: Overview and discussion of a new method for pH monitoring

Junghjem M, Ptok M.
HNO. 2011 Sep;59(9):893-9.

BACKGROUND Extraesophageal reflux disease often requires diagnosis and treatment by a phoniatry or ear, nose and throat specialist. The disease needs to be differentiated from gastroesophageal reflux disease.

OBJECTIVE A new oropharyngeal pH measuring system with a single channel probe has recently been introduced. The aim of this study was to compare oropharyngeal pHmetry with the existing diagnostic methods for extraesophageal reflux disease and to present initial results in our own patients.

METHODS A literature search for oropharyngeal pH-metry was performed in the data-bases NHS EED, HTA, DARE, Clinical trials, Cochrane reviews and Medline/PubMed. A selective literature search was also carried out on the problem of extraesophageal reflux disease.

RESULTS Evaluation scales, trial proton pump inhibitor therapy or pHmetry, for example, can be used to diagnose extraesophageal reflux disease. pHmetry can be performed using a classical two-channel pHmetry system; a new oropharyngeal pH measuring system has recently been introduced. This new method has been evaluated in initial studies for normative data and has been compared to two-channel pHmetry. Prospective randomized studies to diagnose extraesophageal reflux disease with the new oropharyngeal pHmetry method are still lacking.

DISCUSSION Oropharyngeal pHmetry has some potential advantages compared to classical two-channel pHmetry; however, a lot of questions remain unanswered. These will be discussed and illustrated with the help of a number of own patient case reports.

Relationship between gastro-oesophageal reflux and airway diseases: The airway reflux paradigm

Pacheco-Galván A, Hart S, Morice A.

Our understanding of the relationship between gastroesophageal reflux and respiratory disease has recently undergone important changes. The previous paradigm of airway reflux as synonymous with the classic gastro-oesophageal reflux disease (GORD) causing heartburn has been overturned. Numerous epidemiological studies have shown a highly significant association of the acid, liquid, and gaseous reflux of GORD with conditions such as laryngeal diseases, chronic rhinosinusitis, treatment resistant asthma, COPD and even idiopathic pulmonary fibrosis. However, it has become clear from studies on cough hypersensitivity syndrome that much reflux of importance in the Airways has been missed, since it is either non- or weakly acid and gaseous in composition. The evidence for such a relationship relies on the clinical history pointing to symptoms associations with known precipitants of reflux. The tools for the diagnosis of extra-oesophageal reflux, in contrast to the oesophageal reflux of GORD, lack sensitivity and reproducibility. The original methods for measuring pharyngeal pH were not quite right due to technical problems, such as the drying out of the catheter and the accumulation of mucus and food. The Dx-pH Measurement system (Dx-pH; Restech Corporation, San Diego, CA) is a highly sensitive and minimally-invasive device for detecting acid reflux in the posterior pharynx. This sensor detects aerosolised or liquid
acid, resists drying out and its electrical continuity is not impeded by the contact of liquids or tissues. Ayazi S et al. have shown the characteristics of mean pH in the oropharynx of healthy subjects using the Dx-pH catheter. The pharyngeal pH score (RYAN) for abnormal pH (limit of 5.5 for standing and 5.0 in supine position) has been calculated in a way similar to the DeMeester oesophageal score. Furthermore, an alternative scoring system has been developed based on the changes in pH. Wiener et al. compared traditional 24-hour pharyngo-oesophageal monitoring with Dx-pH monitoring in 15 patients with extra-oesophageal symptoms. All the events measured with the Dx-pH method were preceded by and associated with falls in distal oesophageal pH in a progressive anterograde manner. However, oropharyngeal studies with the Dx-pH catheter showed a growing pH gradient from the distal oesophagus to the oropharynx. The oropharynx usually presents a mildly acidic pH, rarely with a pH less than 4. This could help explain why the previous attempts at distinguishing normal subjects from the subgroup of patients with atypical symptoms using quantitative cut-values of pH < 4 have not been reliable.

Laryngopharyngeal Reflux (LPR) in patients with persistent hoarseness

Dymek A, Dymek L, Starczewska-Dymek L, Bożek A, Dymek T, Nowak K.

INTRODUCTION In 2006 the Global Consensus Group in Montreal confirmed that reflux laryngitis is evidence-based related with Gastroesophageal Reflux Disease (GERD).

AIM To evaluate the frequency of LPR in selected group of patients with chronic hoarseness. We were also interested in assessment of the relationship between Reflux Symptoms Index (RSI) scores, RYAN scores from the pharyngeal pH monitoring and the morphological changes in the larynx according to Reflux Findings Score (RFS). In addition, we wanted to assess the frequency of various clinical symptoms included in the RSI questionnaire among patients with LPR.

MATERIALS AND METHODS 42 patients from an outpatient ENT clinic with chronic hoarseness and RSI ≥13. All subjects underwent pharyngeal pH monitoring with the Dx-pH System Restech™ and laryngoscopy.

RESULTS Among 42 patients with chronic hoarseness, LPR was confirmed in 35 patients (83.33%). In 7 subjects pharyngeal pH monitoring was normal. Among all patients with confirmed LPR, only 5 out of 8 elements of RFS laryngoscopic changes were found. The most frequent inflammatory changes observed included erythema of the arytenoids and interarytenoid regions (posterior laryngitis).

These findings were found in 30/35 patients with LPR. Median value of RFS in patients with LPR was 4.45, which is lower than the cut off value of 7 necessary for recognition of LPR. There is statistically significant positive correlation between RYAN scores and the RFS scale results (correlation coefficient 0.91, p<0.001).

CONCLUSIONS Pharyngeal pH monitoring confirmed LPR in 83.33% selected group of patients with chronic hoarseness and RSI 13. Isolated erythema of arytenoid and interarytenoid region was the most frequent inflammatory abnormality found in the larynx. RFS values below 7 do not exclude the diagnosis of LPR. We can use RFS scales as a prognostic test of severity of LPR – due to statistically significant positive correlation between RYAN score and RFS values. The use of RSI scale revealed that the most frequent symptom among patient with LPR was throat clearing followed by hoarseness.

Histologic vs. pH probe results in laryngopharyngeal Reflux

Andrews T.

OBJECTIVE Laryngopharyngeal reflux (LPR) is well documented in children. However, methods of obtaining accurate diagnosis are controversial. As a prelude to establishing normative values in children, we retrospectively reviewed comparison data of 63 consecutive children tested by pH probe and postcricoid biopsy.

METHOD Sixty-three consecutive patients with symptoms of reflux without evidence of sinusitis, allergic rhinitis, or adenoid disease were studied by pH probe (Restech Dx Measurement System, San Diego, California) simultaneous with posterior cricoid biopsy (our previous diagnostic method). All testing was done through outpatient ambulatory surgery under general anesthesia.

RESULTS Of the 63 total patients (age 6 months-17 years), 37 (60%) were positive for reflux by probe with a negative biopsy. Eleven (17%) tested negative to probe and biopsy. Ten (15%) were excluded (pulled probe). Five (8%) were positive by probe and biopsy.

CONCLUSION Normative values in children have not been determined in this instrument. We believe it may offer a satisfactory diagnostic tool. These results, and previous studies, suggest that pH probe testing is superior to histologic diagnosis in determining LPR. However, normative values must be determined in children prior to further comparative studies.
Evaluation of laryngopharyngeal reflux in pediatric patients with asthma using pharyngeal pH monitoring: The impact of a new technique

Banaszkiewicz A, Dembinski L, et al.
Advances in Pneumology, Bonn, Germany, 2011.

OBJECTIVE There is constant discussion about the association between asthma and gastroesophageal and/or laryngopharyngeal reflux. Pharyngeal pH-monitoring is a new technique that allows a physician to check whether reflux really crosses the upper oesophageal sphincter barrier. The aim of the study was to assess the prevalence of laryngopharyngeal reflux (LPR) in children with difficult-to-treat asthma.

METHODS This was an open, prospective study. All patients were asked to fill out a Reflux Symptoms Index questionnaire. In all children, 24-hour pharyngeal pH monitoring was performed using the Dx-pH Measurement System. LPR was diagnosed on the basis of abnormal values in the composite score (RYAN Score), according to the DeMeester criteria. To verify the hypothesis that the reflux is present in 56% to 68% of asthmatic patients, a sequential test was used.

RESULTS A total of 21 subjects (mean age of 12.74 years old) were enrolled in the study. Laryngopharyngeal reflux was diagnosed in 13 (61.9%) children. The prevalence of LPR was between 56% and 68%. No association was found between the diagnosis of reflux and anthropometric data, spirometry results, age of asthma diagnosis and total IgE level. There was a positive correlation between LPR diagnosis and the degree of asthma control (77% vs. 12.5% at the 4th step of asthma treatment, \(p=0.0121\)). LPR was more frequent in higher fluticasone dose users as compared with lower dose users (\(p=0.01977, \text{OR}=17.27\)) and in montelukast users as compared with nonusers (\(p=0.0075, \text{OR}=19\)). The mean Reflux Symptoms Index score was almost two times higher in patients with reflux as compared with those without reflux (13.2 vs. 6.75, respectively, \(p=0.00337\)).

CONCLUSION The prevalence of laryngopharyngeal reflux in children with difficult-to-treat asthma is high (between 56% and 68%).

Oropharyngeal pH monitoring for the detection of extraesophageal manifestations of gastroesophageal reflux in children

Burpee T, Christie D. J

BACKGROUND AND AIMS Verification of gastroesophageal reflux (GER) as the cause of extraesophageal symptoms is challenging. The Restech Dx-pH pharyngeal probe can measure both liquid and aerosolized pH in the pharynx. Our aim was to assess the tolerance of this probe in children and to gain pilot data of the correlation between pharyngeal acid exposure and upper respiratory and oropharyngeal complaints.

METHODS We performed 24-hour oropharyngeal pH monitoring in 27 children (aged 15 months to 16 years) with extraesophageal complaints suspected to be due to GER, including dental enamel erosions (n=1/47), chronic sinusitis (n=1/45), vocal hoarseness (n=1/41), and chronic lung disease (n=1/414) (Table 5). Noted GER symptoms included regurgitation, vomiting, heartburn, and upper abdominal pain. Based on published Restech Dx-pH adult normal values, reflux events were defined as a pH drop below 5.5 when upright and below 5.0 when supine. Number and duration of events and percent time in reflux were calculated. As pediatric values are lacking, published adult discriminatory values were used to determine those with an abnormal pharyngeal pH environment.

RESULTS The probe was well tolerated in all 27 patients. The number of children with increased pharyngeal acid in each complaint group, stratified by the presence or absence of GER symptoms, is displayed below.

CONCLUSIONS The Restech Dx-pH oropharyngeal probe is well tolerated in children. The presence or absence of GER symptoms is not predictive of pharyngeal acid exposure, and pharyngeal acid does not always explain upper respiratory and oropharyngeal complaints. Further studies, including normative pH values, are needed in children.

Proton-pump inhibitor therapy induces acid-related symptoms in healthy volunteers after withdrawal of therapy

Reimer C, Søndergaard B, Hilsted L, Bytzer P.

BACKGROUND AND AIMS Rebound acid hypersecretion (RAHS) has been demonstrated after 8 weeks of treatment with a proton-pump inhibitor (PPI). If RAHS induces acid-related symptoms, this might lead to PPI dependency and thus have important implications.

METHODS A randomized, double-blind, placebo-controlled trial with 120 healthy volunteers was conducted. Participants were randomized to 12 weeks of placebo or 8 weeks of esomeprazole 40 mg/d followed by 4 weeks with placebo. The Gastrointestinal Symptom Rating Scale (GSRS) was filled out weekly. A score of >2 on 1 of the questions regarding heartburn, acid regurgitation, or dyspepsia was defined as a clinically relevant acid-related symptom.
RESULTS There were no significant differences between groups in GRS scores at baseline. GRS scores for acid-related symptoms were significantly higher in the PPI group at week 10 (1.4 +/- 1.4 vs 1.2 +/- 0.9; P = .023), week 11 (1.4 +/- 1.4 vs 1.2 +/- 0.9; P = .009), and week 12 (1.3 +/- 1.2 vs 1.0 +/- 0.3; P = .001). Forty-four percent (26/59) of those randomized to PPI reported > or = 1 relevant, acid-related symptom in weeks 9-12 compared with 15% (9/59; P < .001) in the placebo group. The proportion reporting dyspepsia, heartburn, or acid regurgitation in the PPI group was 13 of 59 (22%) at week 10, 13 of 59 (22%) at week 11, and 12 of 58 (21%) at week 12. Corresponding figures in the placebo group were 7% at week 10 (P = .034), 5% at week 11 (P = .013), and 2% at week 12 (P = .001).

CONCLUSIONS PPI therapy for 8 weeks induces acid-related symptoms in healthy volunteers after withdrawal. This study indicates unrecognized aspects of PPI withdrawal and supports the hypothesis that RAHS has clinical implications.

Empiric treatment of laryngopharyngeal reflux with proton pump inhibitors: a systematic review

Karkos PD, Wilson JA.

OBJECTIVE The objective of this study was to define the outcome of empiric treatment of suspected laryngopharyngeal reflux (LPR) symptoms with proton pump inhibitors (PPIs)

DESIGN The authors conducted a systematic review of the English and foreign literature. Studies that used PPIs as an empiric treatment modality for suspected LPR, whether alone or in combination with other acid suppressants and/or placebo, were included. Studies that did not include PPIs as a treatment option were excluded.

MAIN OUTCOME MEASURES A lack of common outcome measures was evident in the uncontrolled studies. In the randomized, controlled trials, outcome measures included symptom questionnaires and videolaryngoscopy. Only one study used computerized voice analysis.

RESULTS Fourteen unblinded, nonrandomized study with a control group of healthy volunteers and six double-blind, placebo-controlled randomized trials were identified from 1994 to 2004. Selection bias, blinding of the results, and lack of common outcome measures were some of the problems preventing a formal metaanalysis. Although uncontrolled series reported positive results, randomized, controlled trials demonstrated no statistically significant differences for changes in severity or frequency of symptoms associated with suspected reflux between PPIs and placebo.

CONCLUSIONS Recommendations for empiric treatment of suspected LPR with PPIs, by far the most common ear, nose and throat practice in the United Kingdom, are based on poor levels of evidence from uncontrolled studies. The few randomized, controlled trials have failed to demonstrate superiority of PPIs over placebo for treatment of suspected LPR.

Activity/stability of human pepsin: implications for reflux attributed laryngeal disease

Johnston N, Dettmar PW, Bishwokarma B, Lively MO, Koufman JA.

OBJECTIVES/HYPOTHESIS Exposure of laryngeal epithelia to pepsin during extra-esophageal reflux causes depletion of laryngeal protective proteins, carbonic anhydrase isoenzyme III (CAIII), and squamous epithelial stress protein Sep70. The first objective of this study was to determine whether pepsin has to be enzymatically active to deplete these proteins. The second objective was to investigate the effect of pH on the activity and stability of human pepsin 3b under conditions that might be found in the human esophagus and larynx.

STUDY DESIGN Prospective translational research study.

METHODS An established porcine in vitro model was used to examine the effect of active/inactive pepsin on laryngeal CAIII and Sep70 protein levels. The activity and stability of pepsin was determined by kinetic assay, measuring the rate of hydrolysis of a synthetic pepsin-specific substrate after incubation at various pH values for increasing duration.

RESULTS Active pepsin is required to deplete laryngeal CAIII and Sep70. Pepsin has maximum activity at pH 2.0 and is inactive at pH 6.5 or higher. Although pepsin is inactive at pH 6.5 and above, it remains stable until pH 8.0 and can be reactivated when the pH is reduced. Pepsin is stable for at least 24 hours at pH 7.0, 37 degrees C and retains 79% +/- 11% of its original activity after reacidification at pH 3.0.

CONCLUSIONS Detectable levels of pepsin remain in laryngeal epithelia after a reflux event. Pepsin bound there would be enzymatically inactive because the mean pH of the laryngopharynx is pH 6.8. Significantly, pepsin could remain in a form that would be reactivated by a subsequent decrease in pH, such as would occur during an acidic reflux event or possibly after uptake into intracellular compartments of lower pH.