

THE VISIBLE VOICE

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LARYNGOPHARYNGEAL REFLUX A RELIGIOUS WAR

[Jamie A. Koufman, M.D., F.A.C.S.](#)

When it comes to LPR, I'm an elder statesman. I have been interested in *laryngopharyngeal reflux* (LPR), the backflow of gastric (stomach) contents into the throat, my entire career.¹⁻³⁶ I actually coined the term *laryngopharyngeal reflux* more than two decades ago to help distinguish it from classical *gastroesophageal reflux disease* (GERD). In the intervening years, the manifestations, mechanisms, diagnosis and treatment of LPR have been studied by many; but after all this time, there is more controversy than ever.

LPR is a high-prevalence disease; but there is no generally-accepted diagnostic gold standard. Consequently there are no well-accepted therapeutic endpoints. The problem of nebulous diagnosis is compounded by the fact that patients with LPR – with symptoms of hoarseness, chronic cough, and difficulty swallowing -- may be seen by many different types of doctors (e.g., primary care, otolaryngology, gastroenterology) with different points of view. Nevertheless, LPR is generally felt to be an otolaryngologic disease and GERD generally gastrointestinal.

Divergence between the specialties can be blamed in part on inadequate cross-pollination of the medical literature, in part because of misleading and/or flawed LPR research, and in part because of medical economic (“turf”) issues. LPR has become like a religious war with disbelievers raging against believers. To a great extent, the root of the conflict is the mistaken belief that LPR and GERD are the same disease. This war sometimes puts ailing patients in the middle.

The purpose of this article is to examine why LPR remains enigmatic and to encourage interdisciplinary clinical and basic science research, especially cell biology. This is not a methodical or comprehensive literature review; my intension here is to share my experience, perspective, and insight having worked in this field for half a lifetime

Silent Reflux

LPR is often called *silent reflux*, because the majority of LPR sufferers don't have heartburn, the primary symptom of GERD.^{2-5,21} We examined the esophagi of 58 consecutive patients with pH-documented LPR²² (few of whom ever experienced heartburn) and found that only 12% had

esophagitis and 7% had Barrett’s esophagus; thus, 81% had normal esophageal examinations. All 58, however, did have laryngeal findings of LPR and abnormal pH-monitoring tests.²²

LPR may be epidemic in America; but no one knows for sure. The uncertain prevalence is related to the tricky diagnosis. Chronic cough, for example, is the most common complaint for which people seek medical attention in the United States, but the relationship between silent reflux (LPR) and chronic cough is also unknown.

A few years ago, at Wake Forest (Unreported data 2004-5), we performed impedance reflux-testing on 50 consecutive patients with chronic cough; 68% (34/50) had documented reflux in association with cough. LPR may be an important cause of chronic cough, asthma, sore throat, hoarseness, and sinus disease; but we don’t yet know how to test the premise that LPR is a major risk factor for those diseases.

While LPR and GERD are both due to the adverse impact of acid and pepsin (gastric juices) on tissue, that’s where the similarity ends. The mechanisms, patterns, and manifestations of LPR and GERD are different;^{2-7,14,16,21,22,27,28} see **Table 1**.

TABLE 1: TYPICAL DIFFERENCES BETWEEN LPR AND GERD

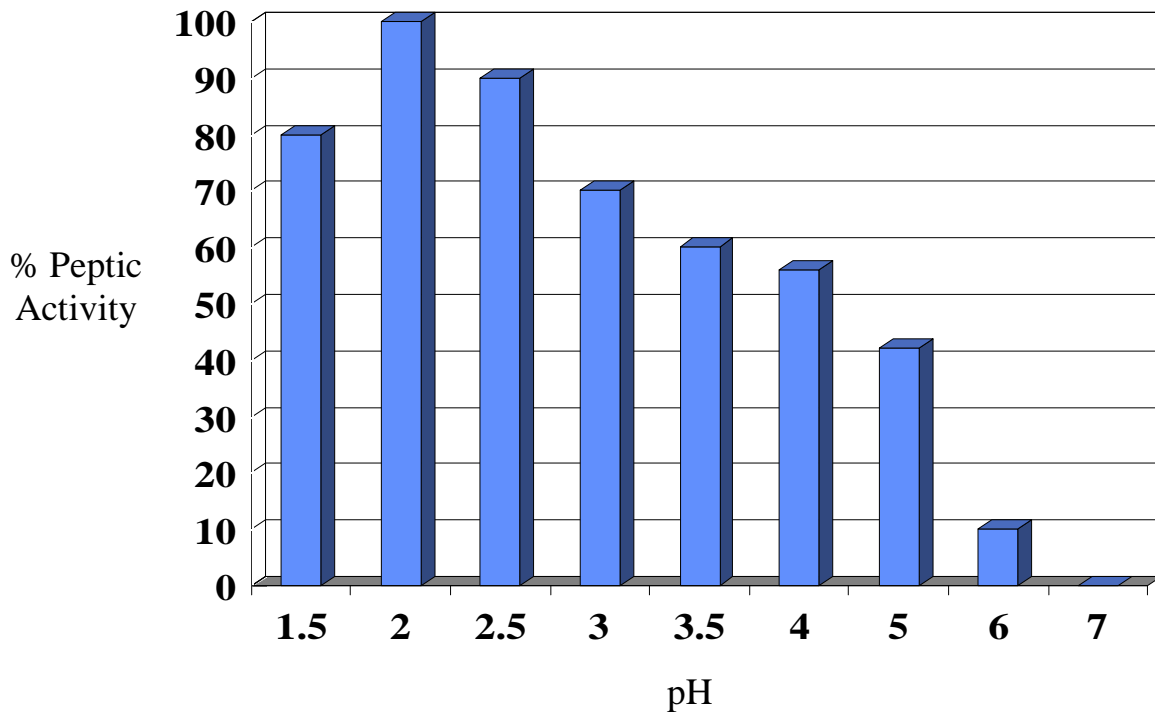
	GERD	LPR
Symptoms		
Heartburn and/or regurgitation	++++	+
Hoarseness, cough, dysphagia, globus	+	++++
Findings		
Esophagitis	+++	+
Laryngeal inflammation	+	++++
Test Results		
Erosive esophagitis or Barrett’s	+++	+
Abnormal esophageal pH monitoring	++++	++
Abnormal pharyngeal pH monitoring	+	+++
Esophageal dysmotility	+++	+
Pattern of Reflux		
Supine (nocturnal) reflux	++++	+
Upright (daytime) reflux	+	++++
Both (Abnormal upright and supine reflux)	+	++
Response to Treatment		
Effectiveness of dietary and lifestyle modifications	++	+
Successful treatment with single-dose PPIs*	+++	+
Successful treatment with twice-daily PPIs*	++++	+++

*PPIs = Proton pump inhibitors

It's Pepsin, Not Acid, that Damages Tissue

The popular belief that stomach acid causes reflux-related tissue injury is incorrect.⁵ In fact, the gastric refluxate has two main components, acid and pepsin; and pepsin (not acid) is the main problem.^{5,11,23,33} This is true for the esophagus and the larynx, and again it appears that the pH thresholds for injury are different.²³ Not only that, it now appears that low (but significant) levels of peptic activity remain even at pH as high as 6.0.³³ The human pepsin activity curve, its percent activity at each pH level, is shown by **Figure 1**.

FIGURE 1: HUMAN PEPSIN ACTIVITY CURVE³³



Cell Biology of LPR

One of the most significant and overlooked differences between LPR and GERD is that the threshold for reflux-related injury of the laryngeal epithelium (lining membrane) is quite low compared to that of the esophagus.^{5,23,33} The esophagus is biologically equipped to defend against reflux, but larynx is not, and the magnitude of difference may help explain why special new criteria are needed to diagnose LPR. Using pH monitoring criteria, up to 50 reflux episodes/day in the esophagus (occurring mostly after meals) are considered normal; but in the larynx, just three reflux episodes a week are probably too many.⁵

Human and animal research confirms that: (1) Pepsin is the primary injurious component of the refluxate; (2) Pepsin is active (proteolytic) above pH 5; and (3) When active pepsin binds to laryngeal epithelium, it is associated with a cascade of adverse consequences, in particular the depletion of key protective proteins^{23,25,26,29-31,33,34}; see **Table 2** below.

TABLE 2: HUMAN TISSUE PROTEIN PROFILE OF CONTROLS, LPR, AND CANCER

	Controls (N=20)	LPR (N=20)	Cancer (N=5)
Pepsin positive (Western blot)	5% (1/20)	95% (19/20)	100% (5/5)
Carbonic Anhydrase III			
E-Cadherin			
SEP70			
SEP53			
HSP70			

= Normal range; = Decreased

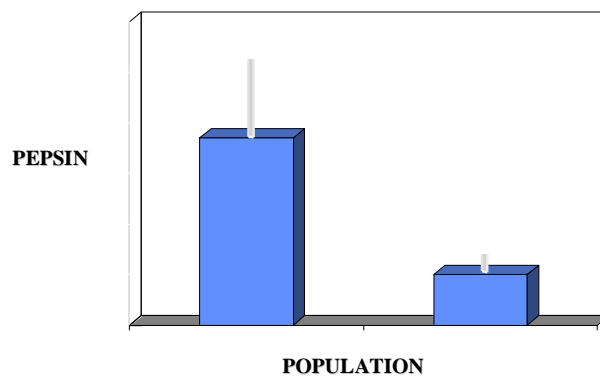
It is important to note that the Western blot method measures tissue-bound (not surface) pepsin. In other words, the pepsin detected by this technique is attached to the cell membrane or it is intracellular.²⁵ LPR and laryngeal cancer have remarkably similar profiles; and HSP70 appears to be a differentiating protein (that may turn out to be an excellent marker for carcinoma).

The above pepsin-activity and tissue-profile data are provocative from the standpoint of understanding airway disease, and they also call into question the notion of “threshold diagnosis.” It seems doubtful that reflux events at or below one particular measurement level of acidity (i.e., a pH threshold) would or should consistently correlate with (or predict) disease.

In gastroenterology, the accepted threshold for esophageal injury is pH<4.0 despite the fact that that level was selected relatively arbitrarily by Johnson and DeMeester more than 30 years ago.³⁷ When prolonged esophageal pH monitoring became popularized, pH<4.0 was selected because it was believed that pepsin was not active above pH 4.0, and because symptomatic GERD patients undergoing pH monitoring often experienced heartburn with reflux below pH 4.0.³⁸

LPR is the exception that begs the rule. In 1996, using a hemolytic (modified Anson) method, we measured pepsin in the airway secretions of 88 patients with clinical LPR who had undergone ambulatory 24-hour (simultaneous pharyngeal and esophageal) pH monitoring and 12 controls; see below.³⁹

FIGURE 2: PEPSIN LEVELS (MEASURED BY HEMOLYTIC ASSAY) IN THE AIRWAY SECRETIONS OF 88 LPR PATIENTS AND 12 CONTROLS (1996)



B. Abnormal

pH	<1	<2	<3	<4	<5	<6	>6	
PIC*	0.80	1.00	0.70	0.55	0.40	0.10	0.00	
Min.	0	10	30	100	200	100	1000	
RIP	0	10	21	55	80	10	0	RIS = 176

C. Abnormal

pH	<1	<2	<3	<4	<5	<6	>6	
PIC*	0.80	1.00	0.70	0.55	0.40	0.10	0.00	
Min.	10	30	100	200	400	500	200	
RIP	8	30	70	110	160	50	0	RIS = 440

D. Abnormal

pH	<1	<2	<3	<4	<5	<6	>6	
PIC*	0.80	1.00	0.70	0.55	0.40	0.10	0.00	
Min.	0	0	0	0	1000	400	40	
RIP	0	0	0	0	400	40	0	RIS = 440

* PIC = *Pepsin injury coefficient* based on the pepsin activity curve (Fig. 1)

Using the RIP/RIS scoring method, it appears that prolonged pharyngeal exposure at weakly acidic pH may be more damaging than shorter periods of exposure at low pH. It is important to remember that RIP/RIS scoring is designed for interpretation of pharyngeal reflux testing. The concept of examining the entire pH profile is appealing, because it avoids the “which threshold?” question. Time will tell whether or not the RIP and RIS prove to be good clinical measures.

More important than the RIP and RIS scoring system is the concept that LPR is not a threshold disease. The relationship between LPR and the laryngeal epithelium is probably interactive with epithelial defenses determining the outcome, namely, health or disease. It also appears that bound pepsin leads to tissue injury; whereas, surface or intraluminal pepsin does not (**Table 2**).

We examined 20 carefully-selected asymptomatic controls (“normals”) for pharyngeal reflux, and we found that 85% had some pharyngeal reflux pH<5 events.⁴⁰ If those subject were truly asymptomatic (which they were), since 95% (19/20) did not have pepsin (Western blot) in laryngeal pinch biopsies,²⁵ then it seemed logical to conclude that healthy tissues does not contain pepsin.

In the past, the presumption was that reflux disease resulted from excessive exposure of tissue to gastric juices. But since virtually everyone has some weakly-acidic LPR, it seems likely that the effluence of the refluxate is less important than epithelial resistance.³⁶

The Internal Environment

The external environment has gotten a lot of attention in the past two decades; however, it is but one component of *the internal environment*. The internal environment is dynamic. **Table 4** summarizes some of the elements of the internal environment. These humoral and cellular elements are under the influence of neuromuscular, hormonal, vascular and genetic control, and they are also interdependent.

The internal environment is the aerodigestive tract conceptualized as an integrated, multicomponent, multifunction biologic system. That is in balance in health seems reasonable; however, surprisingly little is known about how all the elements interact, and specifically which factors and sequences cause decompensation and disease. It seems likely, for example, that LPR predisposes to upper respiratory infection (URI) and *visa versa*. In 2006, I reviewed a series LPR patients diagnosed by pH-monitoring; 26% (15/57) had the onset of their symptoms with a URI [unreported data]. In addition, seemingly important relationships between LPR and reactive airway diseases remain to be elucidated.

TABLE 4: COMPONENTS OF THE INTERNAL ENVIRONMENT

Cells
 Saliva
 Acid and pepsin
 Immunoglobulins
 Inflammatory mediators (e.g., kinins)
 Food and drink (that which is ingested)
 Mucus and mucus breakdown products
 Gastric, bile salts and other digestive enzymes
 The external environment (that which is inhaled/breathed)

The concept of LPR as an uncomplicated all-or-nothing (“threshold”) disease should be abandoned. Within this context, any single pH threshold diagnostic measure seems woefully inadequate. As of this writing, poorly conceived clinical studies (e.g., treatment outcome studies⁴¹) have only further fueled a confusing and anachronistic model of reflux disease.

The challenge for future clinicians and researchers will be to integrate the whole that has been fragmented, and cell biology holds the key. Multidisciplinary translational research is going to unravel the LPR conundrum.

Meanwhile, internal environment concept will spawn development of new diagnostics and therapeutics. In the future, examination of the expectorate for mucus breakdown products, kinins, and immunoglobulins, in addition to pepsin, may make the diagnosis of LPR non-invasive and definitive. As treatment alternatives to acid-suppression, anti-pepsin therapeutics will be possible by: (1) suppression of production, (2) suppression of secretion, (3) prevention of activation of pepsinogen, (4) inactivation of pepsin, and/or (5) prevention of binding of pepsin to tissue.

APPENDIX: USEFUL CLINICAL MEASURES RECOMMENDED BY THE AUTHOR

A. THE REFLUX SYMPTOM INDEX (RSI)

How do the following problems affect you?	0 = No Problem 5 = Severe Problem						RSI
	0	1	2	3	4	5	
Hoarseness or a problem with your voice	0	1	2	3	4	5	
Clearing your throat	0	1	2	3	4	5	
Excess throat mucous or postnasal drip	0	1	2	3	4	5	
Difficulty swallowing food, liquids, or pills	0	1	2	3	4	5	
Coughing after you ate or after lying down	0	1	2	3	4	5	
Breathing difficulties or choking episodes	0	1	2	3	4	5	
Troublesome or annoying cough	0	1	2	3	4	5	
Sensations of something sticking or a lump in your throat?	0	1	2	3	4	5	
Heartburn, chest pain, indigestion, or stomach acid coming up?	0	1	2	3	4	5	

B. THE GLOTTAL CLOSURE INDEX (GCI)

How do the following problems affect you?	0 = No Problem 5 = Severe Problem						GCI
	0	1	2	3	4	5	
Speaking took extra effort	0	1	2	3	4	5	
Throat discomfort or pain after using your voice	0	1	2	3	4	5	
Vocal fatigue (voice weakened as you talked)	0	1	2	3	4	5	
Voice cracks or sounds different	0	1	2	3	4	5	

C. THE REFLUX FINDING SCORE (RFS)

Pseudosulcus	2 Present				
Ventricular obliteration	2 Partial		4 Complete		
Erythema/Hyperemia	2 Arytenoids (only)		4 Diffuse		
Vocal fold edema	1 Mild	2 Moderate	3 Severe	4 Polypoid	
Diffuse laryngeal edema	1 Mild	2 Moderate	3 Severe	4 Obstructing	
Posterior commissure hypertrophy	1 Mild	2 Moderate	3 Severe	4 Obstructing	
Tiger-stripe post-cricoid edema	2 Present				
Thick endolaryngeal mucus	2 Present				
Granuloma/Granulation	2 Present				
Reflux Finding Score					

Comments

With GERD, the symptom heartburn is almost the *sine qua non*, but there is no equivalent LPR symptom. LPR rarely causes a single symptom; and single-symptom outcomes measures usually fall short. I began using the [reflux symptom index](#) (RSI) in about 1982. Now, it is a validated outcomes instrument,¹⁷ but still, there is no threshold number for the surefire diagnosis of LPR.

Recently, I saw a patient with an RSI of 28 who didn't have LPR, and a patient with an RSI of 7 who did. Still, the RSI is an important index (**Table A**). The RSI is especially useful when combined with the *glottal closure index* (GCI) (**Table B**) and the *reflux finding score* (RFS)^{17,18} (**Table C**).

Like the RSI, the GCI is a self-reported symptom index. It is specific for glottal closure problems such as vocal fold paralysis, paresis, presbylaryngis, and striking-zone mass lesions or scarring. It is useful to use the GCI in conjunction with the RSI, because it helps identify patients with problems in addition to LPR, especially those with neuropathic syndromes. The point is that the RSI and GCI measure different things. It is unusual for a patient with LPR alone to have a high (>10) GCI. The GCI is a useful screening tool for glottal closure problems; and it helps prevent the inexperienced clinician from over-diagnosing LPR.

The RFS (**Table C**) also evolved during the 1980s. I should point out that I rarely score for erythema unless it is very obvious, as this appears to be a highly variable and subjective finding that is dependent to a great extent on the lighting during the examination. In my experience, as a diagnostic duo, pseudosulcus and ventricular obliteration seem to work the best.

While the reliable application of the RFS does require practice, I have found that unsophisticated observers can be trained to score larynges with a remarkable degree of consistency and accuracy with thirty minutes of training. When the RFS is used in conjunction with the RSI, the clinical diagnosis of LPR can be made with greater certainty. As a busy clinician who has used both indices every day for virtually every patient visit for more than two decades, I feel that a RSI of >20 combined with a RFS of >10 is virtually diagnostic of LPR.

References

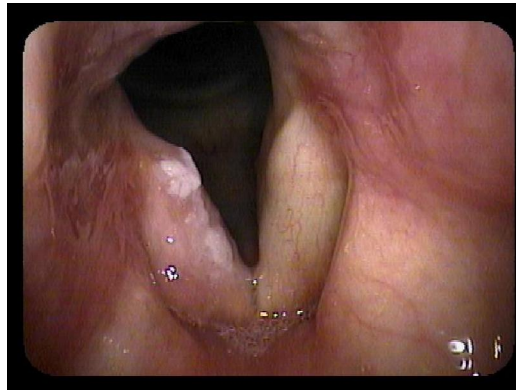
1. Little FB, Koufman JA, Kohut RI, Marshal RB. Effect of gastric acid on the pathogenesis of subglottic stenosis. *Ann of Otol Rhinol Laryngol* 94:516-519, 1985.
2. Wiener GJ, Wu WC, Koufman JA, Copper JB, Richter JE, Castell DO. Laryngeal pathology may be caused by gastroesophageal reflux (GER). An ambulatory 24 hour pH study. *Dig Dis Sci* 31(suppl):515S, 1986.
3. Koufman JA, Wiener GJ, Wu WC, Castell DO. Reflux laryngitis and its sequelae: the diagnostic role of 24-hour pH monitoring. *J Voice* 2:78-89, 1988.
4. Weiner GJ, Koufman JA, Wu WC, Cooper JB, Richter JE, Castell DO. Chronic hoarseness secondary to gastroesophageal reflux disease: Documentation with 24-H ambulatory pH monitoring. *The Amer J of Gastroenterol* 84:12, 1989.
5. Koufman JA. The Otolaryngologic manifestations of gastroesophageal reflux disease (GERD): A clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. *Laryngoscope* 101 (Suppl. 53):1-78, 1991.
6. Koufman JA. Aerodigestive manifestations of gastroesophageal reflux. What we don't yet know. *Chest* 104:1321-1322, 1993.
7. Little JP, Matthews BL, Glock MS, Koufman JA, Reboussin DM, Loughlin CJ, McGuirt Jr. WF. Extraesophageal pediatric reflux: 24-hour double-probe pH monitoring of 222 children. *Ann Otol Rhinol Laryngol Suppl* 169: 1-16, 1997.

8. Koufman JA, Burke AJ. The etiology and pathogenesis of laryngeal carcinoma. *Oto Clin N A* 30:1-19, 1997.
9. Koufman JA, Amin M, Panetti M. Prevalence of reflux in 113 consecutive patients with laryngeal and voice disorders. *Otolaryngol Head Neck Surg* 123:385-388, 2000.
10. Reulbach TR, Belafsky PC, Blalock PD, Koufman JA, Postma GN. Occult laryngeal pathology in a community-based cohort. *Otolaryngol Head Neck Surg* 124:448-450, 2001.
11. Axford SE, Sharp S, Ross PE, Pearson JP, Dettmar PW, Panetti M, Koufman JA. Cell biology of laryngeal epithelial defenses in health and disease: preliminary studies. *Ann Otol Rhinol Laryngol* 110:1099-1108, 2001
12. Duke SG, Postma GN, McGuirt Jr. WF, Ririe D, Averill DB, Koufman JA. Laryngospasm and diaphragmatic arrest in the immature canine after laryngeal acid exposure: a possible model for sudden infant death syndrome (SIDS). *Ann Otol Rhinol Laryngol* 110:729-733, 2001.
13. Belafsky PC, Postma GN, Daniels E, Koufman JA. Transnasal esophagoscopy. *Otolaryngol Head Neck Surg*;125:588-589;2001,
14. Johnson PE, Koufman JA, Nowak LJ, Belafsky PC, Postma GN. Ambulatory 24-hour double-probe pH monitoring: the importance of manometry. *Laryngoscope* 111: 1970-1975, 2001.
15. Smoak BR, Koufman JA. Effects of gum chewing on pharyngeal and esophageal pH. *Ann Otol Rhinol Laryngol* 110:1117-1119, 2001.
16. Postma GN, Tomek MS, Belafsky PC, Koufman JA. Esophageal motor function in laryngopharyngeal reflux is superior to that of classic gastroesophageal reflux disease. *Ann Otol Rhinol Laryngol* 110:1114-1116, 2001.
17. Belafsky PC, Postma GN, Koufman JA. The validity and reliability of the reflux finding score (RFS). *Laryngoscope* 111:1313-1317, 2001.
18. Belafsky PC, Postma GN, Koufman KA. Laryngopharyngeal reflux symptoms improve before changes in physical findings. *Laryngoscope* 111: 979-981, 2001.
19. Belafsky PC, Postma GN, Koufman JA. Validity and reliability of the reflux symptom index (RSI). *J Voice* 16:274-277, 2002.
20. Holland BW, Koufman JA, Postma GN, McGuirt Jr., WF. Laryngopharyngeal reflux and laryngeal web formation in patients with pediatric recurrent respiratory papillomas. *Laryngoscope* 112:1926-29, 2002.
21. Koufman JA, Aviv JE, Casiano RR, Shaw GY. Position statement of the American Academy of Otolaryngology-Head and Neck Surgery on laryngopharyngeal reflux. *Otolaryngol Head Neck Surg* 127:32-35, 2002.
22. Koufman JA, Belafsky PC, Daniel E, Bach KK, Postma GN. Prevalence of esophagitis in patients with pH-documented laryngopharyngeal reflux. *Laryngoscope* 112:1606-1609, 2002.

23. Johnston N, Bulmer D, Gill GA, Panetti M, Ross PE, Pearson JP, Pignatelli M, Axford A, Dettmar PW, Koufman JA. Cell biology of laryngeal epithelial defenses in health and disease: Further studies. *Ann Otol Rhinol Laryngol* 112:481-491, 2003.
24. Westcott CJ, Hopkins MB, Bach KK, Postma, GN, Belafsky, PC, Koufman, JA. Fundoplication for laryngopharyngeal reflux. *J Amer Coll Surg* 199:23-30 2004.
25. Johnston N, Knight J, Dettmar PW, Lively MO, Koufman J. Pepsin and carbonic anhydrase isoenzyme III as diagnostic markers for laryngopharyngeal reflux disease. *Laryngoscope* 114:2129-34, 2004.
26. Knight J, Lively MO, Johnston N, Dettmar PW, and Koufman J. Sensitive pepsin immunoassay for detection of laryngopharyngeal reflux. *Laryngoscope* 115:1473-78, 2005.
27. Carrau RL, Khidr A, Gold KF, Crawley JA, Hillson EM, Koufman JA, Pashos CL. Validation of a quality-of-life instrument for laryngopharyngeal reflux. *Arch Otolaryngol Head Neck Surg* 131:315-20, 2005.
28. Halum SL, Postma GN, Johnston C, Belafsky PC, Koufman JA. Patients with isolated laryngopharyngeal reflux are not obese. *Laryngoscope* 115:1042-5, 2005.
29. Johnston N, Dettmar PW, Lively MO, Postma GN, Belafsky PC, Birchall M, Koufman J. Effect of pepsin on laryngeal stress protein (Sep70, Sep53, and Hsp70) response: Role in laryngopharyngeal reflux disease. *Ann Otol Rhinol Laryngol* 115:47-58, 2005.
30. Gill GA, Johnston N, Buda A, Pignatelli M, Pearson J, Dettmar PW, and Koufman J. Laryngeal epithelial defenses against laryngopharyngeal reflux (LPR): investigations of pepsin, carbonic anhydrase III, pepsin, and the inflammatory response. *Ann Otol Rhinol Laryngol* 114:913-921, 2005.
31. Johnston N, Dettmar PW, Lively MO, and Koufman JA. Effect of pepsin on laryngeal stress protein (Sep70, Sep53, and Hsp70) response: Role in laryngopharyngeal reflux disease. *Ann Otol Rhinol Laryngol* 115:47-58, 2006.
32. Halum SL, Postma GN, Bates DD, Koufman JA. Incongruence between histologic and endoscopic diagnoses of Barrett's esophagus using transnasal esophagoscopy. *Laryngoscope*. 116:303-6, 2006.
33. Johnston N, Dettmar PW, Bishwokarma B, Lively MO, Koufman JA. Activity/stability of human pepsin: implications for reflux attributed laryngeal disease. *Laryngoscope*. 117:1036-9, 2007.
34. Rees LE, Pazmany L, Gutowska-Owsiak D, Inman CF, Phillips A, Stokes CR, Johnston N, Koufman JA, Postma G, Bailey M, Birchall MA. The mucosal immune response to laryngopharyngeal reflux. *Am J Respir Crit Care Med*. 177:1187-93, 2008.
35. Amin MR, Postma GN, Setzen M, Koufman JA. Transnasal Esophagoscopy: A Position Statement from the American Bronchoesophagological Association (ABEA). *Otolaryngol Head Neck Surg* 138:411-13, 2008.
36. Koufman JA. "From silence to omnipresence: Perspective on the evolution of laryngopharyngeal reflux." Chapter from *Classics in Otolaryngology*. Edited by Sulica L & Branski R (In press)

37. Demeester TR, Johnson LF, Joseph GJ, *et al.* Patterns of gastroesophageal reflux in health and disease. *Ann Surg* 184:459-70, 1976.
38. Johnson LF (Personal communications) 2004
39. Koufman JA (Unpublished Data) 1996
40. Koufman JA, Wright SC, Lively MO, Johnston WC, Johnston N, Bishwokarma B, Postma GN. Normal values for pharyngeal pH monitoring. Presented at the annual meeting of the American Laryngological Association, Combined Otolaryngology Spring meetings, Chicago, IL. May 19, 2006 (Submitted for publication).
41. Vaezi MF, Richter JE, Stasney CR, *et al.* Treatment of chronic posterior laryngitis with esomeprazole. *Laryngoscope*. 116:1717-8, 2006.

CASE OF THE MONTH



What is the lesion?

- A. Lichen planus
- B. Candida albicans
- C. Pilia vulgarus
- D. Erythoplakia
- E. Carcinoma

Answer next month

[Answer for last case, August 2008 – A. Granulomas]

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