Laryngopharyngeal Reflux (LPR)
a.k.a. “Silent Reflux”:
A Not So Silent Disease

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Typical LPR Symptoms

- Hoarseness / dysphonia (71%)
- Cough (51%)
- Globus pharyngeus (throat lump sensation) (47%)
- Frequent throat clearing (42%)
- Mild dysphagia / posterior pharynx edema (35%)
- Wheezing
- Sore throat
- Excessive throat mucus
- Post-nasal drip
- Post-prandial rhinorrhea
Uncommon Symptom in LPR

- HEARTBURN
- Hence, “Silent Reflux”

- Only 35% of patients with LPR have heartburn;
  - Only 25% with esophagitis
    (Laryngoscope 1991;101:1)

- Up to 38% had normal esophageal pH test
  (Am J Gastroenterol 1990;85:38-40 and
LPR Complications

- Adult-onset asthma
- Interstitial lung disease
- Recurrent bronchitis
- Recurrent pneumonia
- Recurrent sinusitis
- Accelerated loss of tooth enamel
- Paradoxical vocal cord dysfunction
- Laryngeal spasm
- Subglottic stenosis
- Vocal cord granulomas and polyps
- Laryngeal CA (without history of smoking or alcohol use)
Atypical LPR Manifestations

- Interscapular burning pain
- Left arm burning sensation
- Chronic mouth and lip burning sensation
- Clicking sound in throat
- Anosmia
- Tinnitus
- Hearing loss

**Maggots crawling out of nostrils !!!**
Pathophysiology

- **Direct mechanism**: caustic acid and pepsin irritation
  - Dense neural blanket in larynx protects against aspiration
  - Sensory deficit in those with laryngeal edema (reversible)

- **Indirect mechanism**: irritation of esophagus evoking laryngeal reflexes that causes vagally-mediated change (bronchoconstriction / cough and mucus accumulation / throat clearing)
Risk Factors

- Obesity or acute weight gain: increase intra-abdominal pressure
- Gastroparesis: *diabetes, pre-diabetes, narcotics use, hypothyroidism, idiopathic*
- Habitual and volitional excessive gastric distension syndrome
- Aerophagia and carbonated beverages: *delivery of gastric acid and enzymes to LP with each burp or belch*
- Hiatal hernia, alcohol, caffeine, peppermints, and chocolates: *lowers resting tone of the upper and lower esophageal sphincters*
- Acidic and spicy foods: *causes direct irritation and inflammation*
- Nicotine: *stimulates acid production*
- Singing, heavy lifting, exercise, and bending over: *prolonged duration and high magnitude of increases in intra-abdominal pressure*
- Gastric outlet obstruction / malignancy
- Sleep apnea
Diagnostic Dilemma

- Easy recognition of multiple manifestations of LPR
- Lack of diagnostic criteria for LPR
- Absence of diagnostic gold standard
- Therapeutic trial not feasible
  - Significant placebo treatment effect
  - Differing measures of treatment response
    - Hoarseness: 3-6 months delay in response
    - Neuropathy: sore throat, mouth burning, anosmia, hearing loss
    - Scarring: interstitial lung disease, subglottic stenosis
    - Co-morbidities: COPD, chronic smoker, allergies
Differential Diagnosis

- Chronic lung disease
- Allergic rhinitis
- Habitual throat clearing
- Tobacco use
- Excessive voice use
- Temperature or climate change
- Emotional issues
- Environmental irritants

*** Consider other causes of symptoms in patients who fail to respond to LPR treatment.
Restech pH Probe

- Minimally invasive catheter for LPR detection
- Measures pH in either liquid or aerosolized droplets at the posterior oropharynx (1cm above UES).
Restech pH Probe Characteristics

- 1.5 mm diameter nasopharyngeal catheter with wireless digital ZigBee™ transmitter
Location of Restech pH Probe Tip

- Restech pH probe distance from the nares: 12.5cm - 13.5cm (Avg. 12.8cm)
- The tear drop shaped tip (3.2 mm) has a colored Light Emitting Diode (LED), for oral visualization.

- The sensor records pH events twice every second (2Hz) and has a hydration monitor to eliminate data if the tip dries out.
No Consensus on Normal pH

- Much less acid exposure is needed to cause injury to the LP than it is to the esophagus
  - Laryngeal epithelium is thin and poorly adapted to deal with caustic injury from pepsin and acid
  - LP lacks the effective stripping motion of esophageal peristalsis and salivary coating (thus, acid and pepsin remain in place longer)
- For GERD, > 50 acid reflux events (pH < 4) per day is abnormal; for LPR, > 4 events (Laryngoscope 1998;108:299-302)

- Pepsin maintains its damaging activity to LP up to a pH of 6 (Ann Otol Rhinol Laryngol 2003;112:481)
Believe It or Not?

- Negative pharyngeal pH probe test does not rule out LPR

- High false-negative tests (20-50%) *(Am J Gastroenterol 1997;92:825-9)*
  - Lack of validated, universally accepted diagnostic criteria for LPR

- **Non-acidic LPR**
Non-acidic LPR

- Bile juice irritation (pH 6.8 to 7.4)
- Pepsin caustic injury
  - Maximal activity at pH of 2
  - Inactive at pH above 6.5
  - It is not fully denatured or irreversibly inactivated until pH of 8.0
- Food, pancreatic juice, and duodenal contents
- Frank aspiration
- Micro aspiration
Risk Factors for Non-acidic LPR

- Achalasia
- Large esophageal diverticulum
- Large hiatal hernia*
- Para-esophageal hernia*
- Gastroparesis*
- Pyloric stenosis*
- Gastric or esophageal malignancy*

* In the setting of PPI use
Multichannel Intraluminal Impedance and pH (MII-pH) Test

- Allows detection of both acid and non-acid GER

- Identifying retrograde liquid (low impedance) or gas (high impedance) movement in the esophagus

- pH monitoring characterizes the acidity of refluxate

- Improve detection of LP reflux and micro-aspiration (JAMA 2005;294:1534 and J Gastrointest Surg 2006;10:54)
Surrogate Tests for NA-LPR

- Upper GI x-ray
- Gastric emptying scan
Role of Restech pH Test in Diagnosing LPR

- pH tests only aids in the diagnosis of LPR. Right now, it is a diagnosis based on clinical history.

- A positive pH test possibly proves the occurrence of LPR, BUT it does not prove causal relationship with symptoms.

- Cause-and-effect can only be established when signs and symptoms of LPR improve or resolve with medical or surgical anti-reflux therapy.

- 6 to 8 weeks lag between treatment and symptom relief.

(Laryngoscope 2001;111:979)
Acid Reflux and Sleep Disturbance

- Shorter sleep duration
- Difficulty falling asleep
- Arousals during sleep
- Poor sleep quality
- Awakening early in the morning
- Obstructive sleep apnea
Mechanisms of Sleep Disturbance in Acid Reflux

- **Esophageal hyperalgesia**
  - Sleep deprivation induces esophageal hyperalgesia to acid perfusion *(J Gastroenterol 2012;47(7):760-9)*

- **Fragmented sleep**
  - Sleep arousal triggers a swallow reflex that leads to esophageal acid clearance.
  - CNS depressing hypnotics (i.e., Zolpidem) increase nocturnal acid exposure time by blunting the arousal and protective swallow reflex. *(Clin Gastro and Hep 2009;7:948-52)*
Factors that Promote Acid Reflux During Sleep

- Delayed gastric emptying
- Reduced esophageal peristalsis
- Decrease in swallowing
- Decrease in salivary secretion
- Prolonged esophageal clearance
- Reduce lower esophageal sphincter tone
Factors that Promote Acid Reflux in OSA

- Resting lower esophageal sphincter (LES) pressure was lower in OSA patients.

- Weakening of the GE junction likely resulted from repetitive strain associated with obstructed breathing events.

Sleep Breath 2011;15(3):561-70
Factors that Promote Acid Reflux in OSA

- Increased negative intrathoracic pressure
- Increased pressure difference between thoracic and abdominal esophagus

*J Otolaryngol 1995;24:238-40*
Cause of Respiratory Symptoms in OSA due to LPR

- Inflammation of the pharynx and larynx leading to narrowing of the lumen due to edema
  
  *Otolaryngol Head Neck Surg 2006;134(5):836-42*

- Local alterations in the mechanoreceptors of the pharynx
  
  *Sleep 2005;28(5):585-93*

- Vagal hyperactivity leading to laryngospasm and bronchoconstriction
  
  *Ear Nose Throat J 2002;81(9Suppl2):2-6*
Obstructive Sleep Apnea (OSA) and Acid Reflux

- OSA can increase the risk of nocturnal acid reflux and vice versa.

World J Gastroenterol 2005;11:839-41*
Obstructive Sleep Apnea (OSA) and Acid Reflux

- Subjects with OSA had frequent nocturnal acid reflux events and symptoms
  - 54 to 89% had signs and symptoms of LPR

*Chest* 1992;101:1539-44
*Braz J Otorhinolaryngol* 2013;79(5):589-93
Obstructive Sleep Apnea (OSA) and Acid Reflux

- Subjects with nocturnal acid reflux had an increase in respiratory symptoms and OSA.

*Chest* 2002;121:158-63
*Respiratory Medicine* 2012;106:459-66
Obstructive Sleep Apnea (OSA) and Acid Reflux

- OSA and LPR co-exist frequently
  - 57% (Eur Arch Otorhinolaryngol 2012;269:2575-80)
  - 61% (Otolaryngol Head Neck Surg 2006;135(2):253-7)
  - 62% (Eur Arch Otorhinolaryngol 2004;261(4):229-32)
Obstructive Sleep Apnea (OSA) and Acid Reflux

- Using simultaneous pH monitoring and polysomnography
- OSA induces acid reflux
  - 53-70% of LPR events occurred during apnea-hypopnea episodes
  
  *Eur Arch Otorhinolaryngol 2012;269:2575-80*
  *Am J Med 2000;108(Suppl 4a);120S-125S*
  *Eur Arch Otorhinolaryngol 2004;261(4):229-32*

- Acid reflux triggers apnea events
  - 27% of apnea events occurred 2 minutes after acid reflux detected

  *Hepato-Gastroenterology 2011;58:1566-73*
OSA and LPR Treatment Effectiveness

- Treatment of OSA with CPAP has shown to improve nocturnal acid reflux

Arch Intern Med 2003;163:41-5
Chest 1992;101:1539-44
Sleep Breath 2011;15(3):561-70
Effect of CPAP on Acid Reflux

- Increased the nadir pressure of the LES during LES relaxation
- Decreased the duration of LES relaxation

Sleep Breath 2011;15(3):561-70
OSA and LPR Treatment Effectiveness

- Treatment of LPR reduced Epworth Sleepiness Scale (ESS) and snoring Visual Analogue Scale (VAS), but did not improve polysomnographic parameters.

- Treatment of OSA with CPAP improved subjective parameters of reflux such as Reflux Symptom Index (RSI) and Reflux Finding Score (RFS), but did not improve objective parameters on 24-hour pH monitoring.

_Eur Arch Otorhinolaryngol 2012;269:2575-80_
Treatment of LPR

- Generally treated with high-dose proton-pump inhibitors
  
  *Am J Gastroenterol* 2001;96:979

- Evidence of efficacy is inconsistent
  
  *Otolaryngol Head Neck Surg* 2004;131:342,
  *Laryngoscope* 2006;116:254, and *Laryngoscope* 2001;111:2147

- Pharyngeal pH monitoring may be needed to monitor adequacy of treatment for hopes of better treatment outcome

- Nissen fundoplication surgery
  - Medical treatment failure, young patients, or patient preference
PPI and Hip Fracture Risk

JAMA 2006;296:2947-53
Recommendations for PPI Users

- Regularly review need for continued treatment
- Continue treatment if indicated; absolute risk is small
- Although practical, there is no official guideline for intensifying osteoporosis screening
- Bone density test every 2 years is acceptable practice
- Calcium 1,000 – 1,200 mg daily
- Vitamin D$_3$ 600 – 1,000 IU daily
Esophageal Adenocarcinoma

- Most rapidly rising incidence cancer in the United States
  
  *JAMA 1991;265:1287-9 and Cancer 1998;83:2049-53*

- Majority are accompanied by underlying intestinal metaplasia (Barrett’s esophagus)
Barrett’s Esophagus and Risk of Adenocarcinoma

- Risk of adenocarcinoma in patients with Barrett’s esophagus is increased in patients with dysplasia
  - No dysplasia – 2%
  - Low-grade dysplasia = 7%
  - High-grade dysplasia = 22%

- Screening EGD is recommended for patients with acid reflux disease
  - The longer the duration of reflux symptoms, the higher the prevalence of BE at the time of EGD
Summary

- Common respiratory, ENT, and allergy symptoms may not always be just what they seem to be.
  - If they fail to respond to conventional treatment, think LPR.
  - If their presentation is outside the norm, think LPR.
  - It also would not hurt to just keep LPR in your differential dx.

- Early recognition and treatment of LPR can save the patient from unwanted complications. Some of which, may be irreversible.

- LPR is treatable in most cases. And if not, it is at least manageable.

- If your clinical suspicion for LPR is high, and your GI colleague does not agree with you, get a second opinion.