LARYNGOPHARYNGEAL REFLUX

Emphasis on Diagnostic and Therapeutic Considerations

Viet Pham, M.D.
Faculty Advisor: Michael Underbrink, M.D.
The University of Texas Medical Branch
Department of Otolaryngology
Grand Rounds Presentation
August 25, 2009

Translation: Argh! My mouth is on fire!
Why won't you help me?!

All images obtained via Google search unless otherwise specified. All images used without permission except for those provided by Dr. Underbrink.

(http://www.smbc-comics.com)
Outline

- Features
- Implications
- Diagnostics
  - Reflux Symptom Index
  - Reflux Finding Score
- Treatment
  - Pharmacology
  - Algorithm
- Controversies
- Conclusion
Laryngopharyngeal Reflux (LPR)

- Other aliases: extraesophageal reflux, reflux laryngitis, posterior laryngitis
- Contributes up to 50% of laryngeal complaints
- Backflow of gastric contacts into larynx, pharynx, and upper aerodigestive tract
- Upper esophageal sphincter (UES) dysfunction
- Affects 50 million Americans
  - Present in 4-10% of those with gastroesophageal reflux disease (GERD)
  - About 20-70% with LPR have symptoms of GERD
Upper Esophageal Sphincter

- C-shaped sling attached to cricoid cartilage
  - Cricopharyngeus
  - Thyropharyngeus
  - Proximal cervical esophagus

- Innervated by pharyngeal plexus
  - Vagus nerve
    - Superior laryngeal nerve
    - Recurrent laryngeal nerve
  - Glossopharyngeal nerve
  - Sympathetics from superior cervical ganglion

NOTES: Cummings, Ch. 109
The motor neurons that control the cricopharyngeus are found in the brainstem in the nucleus ambiguus, and stimulation of the nucleus tractus solitarius (the afferent nucleus of the vagus) results in contraction of the cricopharyngeus. [56] In canine studies, vagal nerve stimulation produced UES relaxation, and sectioning of both vagus nerves produced severe dysphagia. [49] Sensory information from the UES is transmitted via the glossopharyngeal nerve and the sympathetic nerves. [56]
Additional Pathophysiology

- Exposure to gastric acid and activated pepsin
  - Direct mucosal damage
  - Impaired mucociliary clearance
    - Postnasal drip
    - Throat clearing

- Less carbonic anhydrase III leads to less bicarbonate ions

- Heterotopic gastric mucosa in cervical esophagus

Immunohistochemical detection of pepsin (Johnston et al, 2004)
Key Symptoms

- Cervical dysphagia
- Globus
- Respiratory complaints
  - Sore throat
  - Chronic cough
  - Throat clearing
- Dysphonia
- Hoarseness
- Upright (daytime) reflux
- Heartburn uncommon
- Normal acid clearance
Comparison to Gastroesophageal Reflux

- Cervical dysphagia
- Globus
- Respiratory complaints
  - Sore throat
  - Chronic cough
  - Throat clearing
- Dysphonia
- Hoarseness
- Upright (daytime) reflux
- Heartburn uncommon
- Normal acid clearance

- Dysphagia
- Less respiratory complaints
- Rare dysphonia
- Supine (nighttime) reflux
- Heartburn
- Delayed acid clearance
- Regurgitation
- Esophagitis
Other Symptoms

- Asthma exacerbation
- Ear pain
- Excess throat mucus
- Halitosis
- Laryngospasm
- Neck pain

- Odynophagia
- Postnasal drip
- Voice complaints
  - Breaks
  - Fatigue
  - Longer warmup time
  - Loss of upper singing range
Physical Findings

- Posterior laryngitis
  - Edema
  - Posterior commissure and arytenoids
    - Increased vascularity
    - Erythema

- Edema
  - Infraglottic (pseudosulcus vocalis)
  - Diffuse

- Ventricular effacement

- Mucosal hypertrophy

- Laryngeal pachydermia (granularity, cobblestone)

- Ulcers, granulomas, scarring, stenosis

(Belafsky et al, 2001)
Implications

- Asthma
- Bronchiectasis
- Cervical dysphagia
- Chronic cough
- Chronic dysphonia
- Chronic laryngitis
- Chronic rhinitis
- Dental caries
- Globus pharyngeus
- Laryngeal carcinoma
- Laryngeal papillomas
- Laryngomalacia
- Laryngospasm
- Laryngotracheal stenosis
- Obstructive sleep apnea
- Otitis media
- Paradoxical vocal-fold motion disorder
- Recurrent croup
- Reinke edema
- Ulceration
- Vocal fold granulomas
Implications: Carcinoma

- Head and neck squamous cell carcinoma
  - Not established as a carcinogen
  - Complication after radiation therapy
  - High incidence of LPR with premalignant and early glottic carcinomas

- Esophageal adenocarcinoma
  - Increased LPR prevalence with increasing disease severity
  - Erosive gastritis in 52% LPR patients compared to 38% GERD patients
  - No set guidelines for esophagoscopy use in LPR
Pediatric Considerations

- Abnormal crying
- Anorexia
- Apnea
- Chronic cough
- Chronic nasal pain
- Dental erosion
- Dysphagia
- Irritability
- Laryngomalacia
- Nasal obstruction
- Otitis media/otalgia
- Recurrent upper respiratory infections
- Regurgitation/vomiting
- Rhinorrhea
- Sleeping disorders
- Subglottic stenosis
- Sinusitis
- Torticollis (Sandifer’s Syndrome)
Diagnosis

- Ambulatory 24-hour double-probe pH monitoring
  - Current standard
  - Probes above upper and lower esophageal sphincters
  - Detects acidic reflux events only

- Impedence
  - Multiple electrode pairs on pH-probe-type catheter
  - Track retrograde bolus transit
  - Measures acidic and nonacidic events

- No set guidelines lead to controversy and misdiagnoses
  - Edema, ventricular effacement, and pseudosulcus vocalis are more common findings
  - Physicians commonly look for posterior laryngitis
- Positive event with pH drop in proximal probe followed by synchronous drop in distal probe
  - pH drop to 4 past UES
  - pH drop to 5 in hypopharynx
  - Longer acid exposure times compared to normal
- Susceptible to false positives
- No difference in sedated and unsedated patients
- Controversy regarding upper probe placement
Reflux Finding Score (RFS)

- Developed by Belafsky, Postma, and Koufman (2001)
- Grades eight separate findings
- Total severity score: 0 to 26
- Score greater than 7 suggests positive dual-probe pH study
  - Statistical likelihood 95%
  - Applicable to asymptomatic individuals
RFS Components

- **Infraglottic edema (pseudosulcus vocalis)**
  0 (absent)    2 (present)

- **Ventricular obliteration**
  0 (none)    2 (partial)    4 (complete)

- **Erythema/hyperemia**
  0 (none)    2 (arytenoids)    4 (diffuse)

- **Vocal fold edema**
  0 (none)    1 (mild)    2 (moderate)    3 (severe)    4 (polypoid)

- **Diffuse laryngeal edema**
  0 (none)    1 (mild)    2 (moderate)    3 (severe)    4 (obstruct)

- **Posterior commissure hypertrophy**
  0 (none)    1 (mild)    2 (moderate)    3 (severe)    4 (obstruct)

- **Granuloma or granulation**
  0 (absent)    2 (present)

- **Thick endolaryngeal mucus**
  0 (absent)    2 (present)
RFS:
Pseudosulcus Vocalis

(courtesy of Dr. Underbrink)
RFS:
Ventricular Obliteration

Posterior commissure hypertrophy

Thick endolaryngeal mucus

Ventricular obliteration

Ventricular obliteration

(courtesy of Dr. Underbrink)
RFS: Erythema/Hyperemia

Vocal fold edema

(courtesy of Dr. Underbrink)
RFS:
Vocal Fold Edema

Posterior commissure hypertrophy

Polypoid chorditis

(courtesy of Dr. Underbrink)
RFS: Laryngeal Edema

Ectatic blood vessels

(courtesy of Dr. Underbrink)
RFS: Posterior Commissure Hypertrophy

Posterior commissure hypertrophy

Nodule

Pseudosulcus vocalis

(courtesy of Dr. Underbrink)
RFS: Thick Endolaryngeal Mucus

Posterior commissure hypertrophy

(courtesy of Dr. Underbrink)
Reflux Symptom Index (RSI)

- Also developed by Belafsky, Postma, and Koufman (2002)
- Validated, self-administered 9-question survey
  - Score: 0 (no problem) through 5 (severe problem)
  - Rank each symptom within the past month
- Score greater than 13 suggests a positive dual-probe pH study
- Scores tend to decrease before physical improvements seen under medical management
## RSI Questions

<table>
<thead>
<tr>
<th>Within the last MONTH, how did the following problems affect you?</th>
<th>0 = No Problem</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Hoarseness or a problem with your voice</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. Clearing your throat</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Excess throat mucous or postnasal drip</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. Difficulty swallowing food, liquids, or pills</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5. Coughing after you ate or after lying down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. Breathing difficulties or choking episodes</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>7. Troublesome or annoying cough</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>8. Sensations of something sticking in your throat or a lump in your throat</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>9. Heartburn, chest pain, indigestion, or stomach acid coming up</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

**TOTAL**
Laryngopharyngeal Reflux Disease Index

- Forty-nine patients with LPR (Beaver et al, 2003)
- Six weeks of proton pump inhibitor therapy
- Comparison of videostroboscopic images
  - Pre-treatment LPR versus controls: 9.50 vs. 2.92
  - Pre-treatment LPR versus post-treatment: 9.50 vs. 7.35
- Blind, randomized evaluation by 3 otolaryngologists
- Twelve scoring items
  - First six considered useful, score: 0 (absent) to 3 (most severe)
  - Last six less useful, few positive scores: 0 (absent) to 1 (present)
Laryngopharyngeal Reflux Disease Index

More Useful
- Posterior supraglottic edema
- Posterior supraglottic erythema
- Vocal fold edema
- Vocal fold erythema
- Subglottic edema
- Subglottic erythema

Less Useful
- Leukoplakia
- Nodules or prenODULES
- Polyps
- Posterior pachydermia
- Webs
- Contact granuloma
Other Diagnostics

- Acidification tests
- Bronchoalveolar lavage
- Esophagogastro-duodenoscopy (EGD)
- Esophagram
- Flexible endoscopic evaluation of swallowing
- Manometry

- Mucosal biopsy
  - Pepsin concentration
  - Carbonic anhydrase III
- Reflux scan
- Spectrophotometric analysis of reflux
  - Bile
  - Pancreatic enzymes
- Voice analysis
Treatment

- Lifestyle modifications
- Pharmacological
- Surgery (fundoplication)
- Symptomatic improvement within 2-3 months on average
Lifestyle Modifications

- Avoid oral intake 2-3 hours before lying supine
- Lay on left side
- Avoidance of aggravating factors
  - Alcohol
  - Caffeine
  - Carbonated beverages
  - Chocolate
  - Citrus
  - Fried food
  - Spicy food
  - Tobacco
- Elevate head of bed
- Weight loss
- Improvement in up to 50% with posterior laryngitis and chronic dysphonia
Pharmacological Treatment

- Counter acid-secretion
  - Antacids
  - Histamine-2 receptor antagonists (H2B)
  - Proton pump inhibitors (PPI)

- Prokinetics
  - Increase lower esophageal sphincter pressure
  - Increase esophageal motility
  - Promote gastric emptying
  - Metoclopramide, bethanacol, domperidone, bromopride

- Sulcrafate for mucosal protection

- Wean patients after 6 months of adequate therapy
H2 Blockers

- Twice-daily regimen is 50% efficacious as PPI
- Best if used before bedtime
  - Histamine regulated spontaneous acid secretion at night
  - Nocturnal acid breakthrough (NAB) controlled with H2B added to twice-daily PPI (Peghini et al, 1998)
- NAB controlled only at beginning of H2B and PPI therapy (Fackler et al, 2002)
- Equivocal difference between twice-daily PPI with or without H2B (Ours et al, 2003)
Proton Pump Inhibitors

- Consensus Conference Report on LPR (1997) recommend twice-daily PPI use for at least 6 months.
- Symptomatic improvement occurs before laryngeal findings (Belafsky, et al, 2001).
- Optimal effect if taken 30-60 minutes before meals.
- Treats acid refluxate only.

<table>
<thead>
<tr>
<th></th>
<th>0 months</th>
<th>2 months</th>
<th>4 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSI</td>
<td>19.3</td>
<td>13.9</td>
<td>13.1</td>
<td>12.2</td>
</tr>
<tr>
<td>RFS</td>
<td>11.5</td>
<td>9.4</td>
<td>7.3</td>
<td>6.1</td>
</tr>
</tbody>
</table>
Proton Pump Inhibitors

- Few placebo-controlled studies
  - Esomeprazole (Reichel et al, 2008)
  - Lansoprazole (El-Serag et al, 2001)
  - Omeprazole (Noordzij et al, 2001)
  - Pantoprazole (Eherer et al, 2003)
  - Rabeprazole (Steward et al, 2004)
  - Esomeprazole (Vaezi et al, 2006)
  - Pantoprazole (Wo et al, 2006)

- Twice-daily PPI superior to daily PPI dosing

- Interarytenoid mucosa and vocal cord abnormalities suggest better response

- Less than 10% remain symptom-free after weaning PPI (Bove, 2006)
Nissen Fundoplication

- Gastric fundus wrapped around esophagus
- Ten-year success rate to treat GERD up to 90%
- Improvement in symptoms and LPR-related physical findings reportedly 73-86%
- Poorer response in those who fail 4 months of medical therapy
Treatment Algorithm

Clinical suspicion for LPR → RSI > 13 and/or RFS > 7 → Empiric therapy: lifestyle modifications, PPI, H2B

3 month follow-up

Symptoms resolved → Titrate PPI and H2B

Symptoms persistent but improved → Increase PPI dose

Symptoms unresponsive → Rule out allergy, non-compliance, alcohol, tobacco, asthma, voice abuse

Definitive assessment: pH monitoring, impedance, EGD

(adapted from Bove, 2006)
Controversies

- Nonspecific symptoms
  - Allergy
  - Asthma
  - Sinusitis
  - Smoking
  - Vocal Abuse

- Diagnostic variability
  - pH probe
  - Poor inter-rater reliability leads to subjective diagnosis
    - No set guidelines for diagnosis
    - Erythema and edema overdiagnosed with fiberoptic laryngoscopy compared to direct laryngoscopy (Milstein et al, 2005)
Controversies: Nonspecific Symptoms

- pH probe-documented LPR in 50% despite LPR symptoms in 69% (Koufman et al, 2000)
- Normal larynx despite symptoms in 17 out of 43 (Ylitalo et al, 2001)
- Asymptomatic LPR
  - At least one LPR sign in 87% healthy people (Hicks et al, 2002)
  - LPR events in 10-30% asymptomatic adults, low acid exposure times (Merati et al, 2005)
Controversies:

- pH Probe

- Controversy regarding upper probe placement
  - Placement 1-2cm above UES allows pH measurement of laryngopharyngeal segment
  - Placement in upper esophagus reduces false-positives from drying

- Negative study does not rule out LPR
  - Positive study in 69% with LPR symptoms and posterior laryngitis (Ylitalo et al, 2001)
  - Positive study in 71% of LPR patients with dual-probe, 98% with triple-probe (Harrell et al, 2005)

- Positive study in normal individuals
  - pH drop in 31% of normal patients (Merati et al, 2005)
  - Up to 10 reflux events over 24-hour period (Vincent et al, 2000)
LPR distinctly defined process separate from GERD

Definitive diagnostic testing is expensive, invasive, and not always available

Evidence to acknowledge relationship between LPR and laryngeal symptoms, if not causality

Empiric treatment with lifestyle modifications and twice-daily PPI 

(http://www.smbc-comics.com)
Acknowledgements

Special thanks to Dr. Underbrink for guidance and provision of videostroboscopic images of LPR findings.
References


Belafsky PC, Postma GN, Koufman JA. Laryngopharyngeal reflux symptoms improve before changes in physical findings. Laryngoscope 2001; 111:979.

Belafsky PC, Postma GN, Koufman JA. The validity and reliability of the reflux finding score (RFS). Laryngoscope 2001; 111:1313.


Fraser AG, Morton RP, Gillibrand J. Presumed laryngopharyngeal reflux: investigate or treat?. J Laryngol Otol 2000; 114:441.


Ing AJ. Cough and gastroesophageal reflux. Am J Med 1997; 103:91S.

Irwin RS. Chronic cough due to gastroesophageal reflux. Chest 1993; 104:1511.


Toohill RJ, Kuhn JC. Role of refluxed acid in pathogenesis of laryngeal disorders. Am J Med 1997; 103:100S.


The End

“I come from the land where the mullet attacks…”

“Business up front…”

“…Party in the back.”

Kountry Gentleman,
Family Force 5