• Up to two-thirds of infants exhibit signs of reflux (Nelson 1997)
• A majority of those children will outgrow their reflux by their second year of age
• Laryngopharyngeal reflux (LPR) has gained increasing recognition as a common pediatric disorder over the past few years.
Classification

- **Physiologic**
  - Infrequent reflux symptoms in the absence of abnormalities
  - Asymptomatic
  - Rarely during sleep
  - Often postprandial

- **Secondary**
  - Neurologic disease or esophageal dysmotility

- **Pathologic**
  - Symptomatic
  - GERD or LPRD
WHAT IS THE DIFFERENCE BETWEEN GERD & LPR?

- **Gastroesophageal reflux (GER)**
  - Retrograde flow of gastric contents into the esophagus

- **Laryngopharyngeal reflux (LPR)**
  - Extraesophageal reflux (EER)
  - Denotes the gastric contents that reaches beyond the upper esophageal sphincter (UES) into oropharynx and/or nasopharynx
## LPR vs. GER

<table>
<thead>
<tr>
<th>LPR</th>
<th>GER</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daytime, upright</strong></td>
<td><strong>Nighttime, supine</strong></td>
</tr>
<tr>
<td>&lt; 10 %</td>
<td>&lt; 22 %</td>
</tr>
<tr>
<td>Normal esophageal motility</td>
<td>Esophageal dysmotility</td>
</tr>
<tr>
<td>Laryngeal/Pharyngeal symptoms</td>
<td>Gastrointestinal symptoms, heartburn</td>
</tr>
</tbody>
</table>
Upper Esophageal Sphincter

- Epiglottis
- Laryngeal opening
- Transverse cricoarytenoid m.
- Posterior cricoarytenoid m.
- Esophageal circular m.
- Esophageal longitudinal m.

Thyroarytenoid m.
Cricothyroid m.
Pathophysiology

- Exact etiology unknown
- Direct acid and/or pepsin injury
- Neural-mediated laryngospasm, throat clearing, coughing
Mucosal injury in LPR

- Laryngeal epithelium more susceptible to damage from refluxate than esophageal epithelium
- Pepsin causes depletion of laryngeal protective proteins and carbonic anhydrase
- Pepsin adhered to laryngeal epithelium can be activated during an acidic reflux episode

Johnston N 2003, 2007
History and Physical

Infants
- Regurgitation/vomiting, dysphagia, anorexia, growth failure, abnormal crying, sleeping disorders, irritability or torticollis (Sandifer’s syndrom)
- Apnea or life-threatening events
- Upper-airway problems: recurrent croup, laryngomalacia, subglottic stenosis
- Chronic respiratory disease

Children
- Laryngotracheal complains: chronic cough, dyspnea, dysphonia
- Pharyngeal complains: persistent sore throat, halitosis, globus sensation, referred otalgia, dental erosion
- Rhinologic complains: nasal obstruction, rhinorrhea, headache
- Chronic respiratory disease
- Gastrointestinal symptoms: regurgitation/vomiting, nausea, chest or abdominal pain, heartburn
Carr et al. 2000

- Retrospective chart review
- 2 groups:
  - 214 children diagnosed with GERD
  - 81 without GERD
- Significant difference in symptoms between groups:
  - Stertor
  - Cyanotic spells
  - Frequent emesis
  - Choking/ gagging
  - Failure to thrive
Symptoms: Infants

Symptoms: Young children

- Abdominal/Belly Pain: p<0.001
- Burping/Belching: p=0.024
- Choking when eating: p<0.001
- Difficulty swallowing: p=0.006
- Refuses to eat: p<0.001
- Vomiting/Regurgitation: p<0.001

Reflux-related Otolaryngologic disorders

- Chronic cough
- Rhinosinusitis
- Laryngitis
- Globus pharyngeus
- Dysphagia
- Airway obstruction
- Apnea
- Asthma
- Recurrent coup
- Laryngomalacia
- Stridor
- Subglottic stenosis
- Vocal cord nodule/granuloma
## Esophageal Biopsy Study

<table>
<thead>
<tr>
<th>Problem</th>
<th>Positive Biopsy (%)</th>
<th>Negative Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>Recurrent croup</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>Cough</td>
<td>81</td>
<td>19</td>
</tr>
<tr>
<td>Apnea</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Stridor</td>
<td>63</td>
<td>27</td>
</tr>
<tr>
<td>Laryngomalacia</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>Subglottic stenosis</td>
<td>68</td>
<td>32</td>
</tr>
<tr>
<td>Post. Glottic edema</td>
<td>81</td>
<td>19</td>
</tr>
</tbody>
</table>

Chronic Rhinosinusitis

- Reflux-induced chronic inflammation of nasal cavity
- Lack of prospective double-blind RCT
- Concurrent role of allergy
- Phipps CD 2000 (EBM B):
  - Higher incidence of GER in sinusitis patients
  - Symptoms improved after GER treatment
- Bothwell MR 1999 (EBM C):
  - 89% (25/28) of sinusitis patients who met criteria for FESS show improvement w/o surgery with GERD treatment
Otitis Media

- Nasopharyngeal inflammation causing Eustachian tube dysfunction
- Crapko 2007
  - Prospective non-randomized
  - Middle ear effusion collected after myringotomy for OME children
  - Pepsin detected in ~ 60% samples
  - pH: 6-7.6 (pepsin inactive)
Chronic cough

- Holinger and Sanders 1991
  - Retrospective
  - 72 children with chronic cough > 1 month and normal chest x-ray
  - Associated with:
    - Asthma (32%), sinusitis (23%), GERD (15%)
Asthma

- Esophageal instillation of acid has been shown to induce bronchospasm and reduce peak flow
- Debley 2006:
  - Prospective cross-sectional study
  - 2397 adolescents
  - GERD 8x more common in asthma patients
  - Higher morbidity (ER/clinic visits, missed school) from asthma if + GERD
Apnea

- Possible mechanisms: Laryngospasm, aspiration, glottic closure reflex
- Herbst 1979
  - Retrospective
  - 14 infants with apneic events and pH probe proven GERD
  - Apnea resolved after GERD treatment
Reflux-induced stridor

• “Pseudo-laryngomalacia”
• Intermittent, not affected by changes in position
• Mechanisms:
  – Acid induced laryngospasm
  – Rapid breathing with esophageal irritation
• Bouchard S 1999:
  – Retrospective
  – 58% of 105 children with stridor and GERD by pH probe
  – 83% of those improve with anti-reflux meds
• Flexible laryngoscopy to evaluate for laryngomalacia
Laryngomalacia

- Most common cause of stridor in infants
- Prolapse of supraglottic tissues into glottis
- Negative pressure created by prolapse causes upward H+ flow
- 50-80% laryngomalacia patients with GERD
- Flexible laryngoscopy
- Direct laryngoscopy and bronchoscopy in prolonged symptomatic patients because of risk of synchronous lesion is 15-30 %
- May perform esophagoscopy and biopsy if airway is robust. Otherwise, perform pH probe
**Subglottic stenosis**

- Acid causes ulceration, basilar hyperplasia, edema of the subglottic mucosa
- Yellon R 1997:
  - Retrospective
  - 80% of 26 children who underwent laryngotracheal reconstruction had at least 1 positive test for GER
  - Barium swallow/ pH monitoring / esophageal biopsy / scintiscan
Diagnostic test for GER/ LPR

- Laryngoscopy
- Bronchoscopy
- Esophagoscopy with biopsy
- Barium Esophagram
- Scintiscan
- **24-hr pH monitoring**
- Esophageal intraluminal impedance
Barium Esophagram

- Used mainly if suspect anatomical abnormalities: Achalacia, web, stricture
- Sensitivity: 20-60%
- Specificity: 64-90%
- Positive predictive value: 80-82%
- Limitation: High false negative rate due to short sampling period
Nuclear Scintigraphy

- Oral ingestion of technetium-labeled food
- Also detects aspiration, non-acidic reflux, and gastric emptying
- Sensitivity: 15-59%
- Specificity: 83-100%
- Limitations:
  - Only measure initial postprandial period
  - Lack of standardized techniques
  - Lack of normative data
Direct Laryngoscopy and Bronchoscopy

- Limited data in Pediatric population
- Carr MM 2001
- Prospective non-RCT
- Indications for DLB: Trach surveillance, persistent stridor, dysphonia, etc.
- 77 children, 50 (65%) GERD +ve based on:
  - pH monitoring
  - Barium esophagram
  - Scintiscan
  - Esophageal biopsy
Example of Laryngeal findings:
- Post-glottic edema
- Arytenoid edema
- TVF edema
- Lingual tonsil enlargement

Cricotracheal findings:
- Edema
- Cobblestoning
- Subglottic stenosis
- Blunting of carina
- Increased secretions

Mild symptom (score = 1), severe (score = 2)
GERD + group has significantly higher laryngeal and/or cricotracheal scores
Score ≥ 7
- Sensitivity: 76%
- Specificity: 86%
Laryngeal Pseudosulcus
Branski et al. 2002

- Prospective randomized blinded trial
- Adult study
- 120 stroboscopic exam of larynx
- Primary complaint of dysphonia x 6 months
- Analyzed by 5 otolaryngologists
- 5-point scale rating
  - Erythema and edema of anterior commissure, vocal folds, arytenoids
  - GER symptoms
## Results of Branski et al.

### Table I.
Summary of Individual Rater Data for Each Measured Descriptive Variable.

<table>
<thead>
<tr>
<th></th>
<th>Rater 1</th>
<th>Rater 2</th>
<th>Rater 3</th>
<th>Rater 4</th>
<th>Rater 5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Edema</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>0.2</td>
<td>0.6</td>
<td>1.2</td>
<td>0.9</td>
<td>0.7</td>
</tr>
<tr>
<td>Membranous folds</td>
<td>1.0</td>
<td>0.9</td>
<td>1.4</td>
<td>1.0</td>
<td>1.4</td>
</tr>
<tr>
<td>Arytenoida</td>
<td>1.1</td>
<td>1.0</td>
<td>0.2</td>
<td>0.5</td>
<td>1.9</td>
</tr>
<tr>
<td>Erythema</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>0.2</td>
<td>0.6</td>
<td>1.3</td>
<td>1.0</td>
<td>1.1</td>
</tr>
<tr>
<td>Membranous folds</td>
<td>0.6</td>
<td>0.8</td>
<td>1.3</td>
<td>1.0</td>
<td>1.4</td>
</tr>
<tr>
<td>Arytenoida</td>
<td>1.1</td>
<td>1.0</td>
<td>0.2</td>
<td>0.6</td>
<td>1.9</td>
</tr>
<tr>
<td>Pachydermia</td>
<td>1.3</td>
<td>1.0</td>
<td>0.5</td>
<td>0.8</td>
<td>1.6</td>
</tr>
<tr>
<td>Severity of GER</td>
<td>1.2</td>
<td>1.0</td>
<td>0.5</td>
<td>0.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Likelihood GER component</td>
<td>1.4</td>
<td>1.2</td>
<td>0.5</td>
<td>0.8</td>
<td>1.7</td>
</tr>
</tbody>
</table>
Esophagoscopy with biopsy

- **Mucosal changes:**
  - Erythema, edema, ulceration, erosion
- **Structural abnormalities:**
  - strictures, webs
- **Histologic esophagitis:**
  - Basal cell hyperplasia, increased papillary height, epithelial inflammation
- **High positive predictive value**
- **Low negative predictive value**
24-hour pH monitoring

- Measure frequency and duration of acid reflux
- Double pharyngoesophageal probe
  - Proximal: 2 cm above UES
  - Distal: 3 cm above LES
- Reflux episode:
  - pH < 4 for 15-30 s
  - Pharyngeal event must be preceded by esophageal event
  - Acid exposure time
24-hour pH monitoring
Little JP 1997

• Prospective study of 222 children
• Age: 1 day – 15 years
• 76 % with abnormal reflux finding at either probe
• 46 % with reflux event at pharyngeal probe but NOT esophageal probe
• Patients with laryngeal abnormalities, and emesis had significantly more pharyngeal acid reflux than patients with non-respiratory symptoms.
Limitations of pH monitoring

– Patient’s factor
  • Inconvenience / discomfort
  • Time consuming
  • Insurance coverage / cost
– May miss intermittent episodes of LPR
– Does not detect non-acidic episodes
– Variability in defining a significant reflux event
Joniau et al. 2007

- Adult study
- Meta-analysis of 11 prospective studies
- 192 normal controls
- 512 reflux laryngitis diagnosed by reflux symptoms index/score
- Double probe 24-hour pH monitoring
- No statistical significance in pharyngeal reflux events between normal and reflux laryngitis groups
- Only 38% reflux laryngitis patients show pharyngeal reflux event in pH monitoring
Multi-channel Intraluminal Impedance (MII)

- Measure impedance produced by flow of food bolus (high ionic content and conductivity) in esophagus
- Able to detect passage of solid, liquid, or gaseous bolus
- Intraluminal impedance rapidly decreases as bolus passes through measuring segment
- Can combine with pH probe to detect acidic and non-acidic episodes
pH probe vs. Impedance

- Rosen R 2006
- Prospective non-randomized
- 25 untreated children, 25 treated with PPI
- Sensitivity in untreated group: No difference (~80% vs. 76%)
- In treated group: sensitivity of impedance group significantly higher (80% vs. 47%)
Empiric treatment of LPR

• Widely used but not validated in Pediatric population

• **Lifestyle modification:**
  – Thickening of feeds
  – Prone positioning
  – Weight loss for older children/adolescent

• **Prokinetic agent:**

• **Acid suppressive therapy:**
  – H2 blocker vs. Proton pump inhibitor (limited data)
Conclusions

- LPR is common among pediatric population and is implicated in many otolaryngologic disorders
- At present, there is no ideal diagnostic tool for pediatric LPR
- Well-designed controlled studies are needed to provide more information for diagnosis and management of pediatric LPR
Thank you!