New Guidelines for Management of Childhood GERD

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Symptoms and Signs of GERD

**INFANT**
- Recurrent regurgitation
- Failure to gain weight?
- Esophagitis
  - Feeding refusal?
  - Irritability?
  - Hematemesis
- Apnea or ALTE?
- Wheezing?
- Recurrent pneumonia
- Upper airway symptoms

**CHILD / ADOLESCENT**
- Recurrent regurgitation
- Esophagitis
  - Hematemesis
  - Heartburn
  - Abdominal pain
  - Dysphagia
- Asthma?
- Recurrent pneumonia
- Upper airway symptoms?

Pathogenic Factors in Esophagitis

**Mechanisms of GER**
- Transient LES relaxation
- Intra-abdominal pressure
- Reduced esophageal capacitance
- Gastric compliance
- Delayed gastric emptying

**Mechanisms of Esophageal Complications**
- Impaired esophageal clearance
- Defective tissue resistance
- Noxious composition of refluxate

**Mechanisms of Airway Complications**
- Vagal reflexes
- Impaired airway protection

Esophageal Acid Clearance

<table>
<thead>
<tr>
<th>Total $^3$H</th>
<th>pH</th>
<th>mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid bolus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dental sucker</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Esophagitis symptoms in childhood

**Esophageal**
- Pain
- Regurgitation
- Dysphagia

**Esophagitis**
- Hematemesis
- Anemia

**ENDOSCOPY**
- Children tend to answer questions in the affirmative making history less reliable
  - Are you having pain? Yes
- The ability to describe and localize pain is highly variable among children
  - Is the pain in your chest? Yes
  - Does the pain feel like burning? Yes
- GERD symptom reports in young children have not been shown to predict disease

Can an accurate diagnosis of GERD be based upon symptoms in children?

Conditions with symptoms that overlap with those of GERD in children

- Eosinophilic Esophagitis
- Infectious Esophagitis
  - Candida
  - HSV
  - CMV
- Ingestions
  - Foreign Bodies
  - Caustic
- Pill Esophagitis
  - Tetracyclines
  - Bisphosphonates
- Anatomic anomalies
  - Strictures
  - Webs
  - Vascular anomalies
- Motility disorders
  - Achalasia
  - Functional Pain Disorders or Non-erosive reflux disease

Symptoms of Eosinophilic Esophagitis by age

In older children and adolescents a history and physical examination are generally sufficient to reliably diagnose GERD and initiate management. (Level C)

In infants and toddlers, and younger children there is no symptom or group of symptoms that can reliably diagnose GERD or predict treatment response. (Level B)
Is Erosive Esophagitis a Chronic Relapsing Disease in Children?

- 48 children age 32-170 mo
- Erosive esophagitis-Henzel Dent grade 2-3 (ulcers or erosions)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Omeprazole (1.4 mg/kg/d) N=48</th>
<th>Ranitidine (10 mg/kg/d) N=16</th>
<th>Placebo N=14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rx X 3 mo</td>
<td>46 healed</td>
<td>Relapse in only 1 pt erosions at 12 mo after initial Rx</td>
<td>3/44 (7%) mild symptoms within 30 months</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Omeprazole 0.7 mg/kg/d N=16</th>
<th>Ranitidine 10 mg/kg/d N=16</th>
<th>Placebo N=14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erosive esophagitis</td>
<td>16</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>Normal mucosa and normal Bx</td>
<td>46</td>
<td>44</td>
<td>42</td>
</tr>
<tr>
<td>Normal mucosa and abnormal Bx</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Treatment of Erosive Esophagitis

- The low rate of relapse, even without maintenance treatment, suggests that different pathophysiologic pathways are probably involved in the mechanisms of Erosive Esophagitis in children.

- Not all reflux esophagitis in children is chronic and relapsing

Approach to the child with possible symptoms of esophagitis

- In younger child (< 8-12 yrs) symptom based diagnosis is unreliable- consider pH probe/ endoscopy?
- Lifestyle
- Consider Empiric RX?
- Symptoms resolve: Wean Rx and Observe
- Symptoms persist: Endoscopy and Biopsy?
- Symptoms recur: Consider on-demand Rx if Sx’s intermittent

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Historically, esophageal biopsy has been used to diagnose GERD in pediatric patients but not in adults.

- Can biopsy be used for the diagnosis of GERD in children with non-erosive disease?
- Is it sensitive and specific?

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Symptoms and histology

1. Overall Symptoms by Age

Orenstein SR, et al. AJG 2006; 101: 628-640

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Pathology in GERD

- The classical histologic parameters of "esophageal inflammation", even when considered together, have a poor correlation with:
  - Symptoms
  - Endoscopic findings
  - Esophageal pH monitoring

both qualitatively and quantitatively in children (Black et al, 1990; Heine et al, 2002; Salvatore et al, 2005)

- Endoscopic biopsy is important to identify or rule out other causes of esophagitis, and to diagnose and monitor Barrett esophagus and its complications.
Approach to the child with symptoms of possible NERD/EERD

- Consider PPI 1-2 mo
- Empiric RX?
- Symptoms resolve: Wean Rx and Observe
- Symptoms persist: Endoscopy and Biopsy

- Normal mucosa and normal Bx: Doubt GERD
- Normal mucosa and abnormal Bx: Erosive esophagitis and Bx c/w GERD
- Possible GERD:
  - Trial PPI?
  - MII/pH testing?
  - Other Dx?

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Etiology of Recurrent Pneumonia

- Retrospective review of 2,952 pneumonia admissions over 10 yrs
- 238 were “Recurrent” pneumonia defined as 2 pneumonia episodes in 1 yr or 3 episodes overall

Owayed AF et al, Arch Pediatr Adolesc Med, 2000

Aspiration From Swallowing or GER?

- Recurrent pneumonia
- Pulmonary fibrosis
- Barium Swallow
- Tc-99m Salivogram

Evaluation of Infant or Child with Recurrent Pneumonia - Is GER the cause?

<table>
<thead>
<tr>
<th>Cause</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration with swallow</td>
<td>48</td>
</tr>
<tr>
<td>Immune disorder</td>
<td>14</td>
</tr>
<tr>
<td>Cong Heart disease</td>
<td>9</td>
</tr>
<tr>
<td>Asthma</td>
<td>8</td>
</tr>
<tr>
<td>Respiratory tract anomalies</td>
<td>8</td>
</tr>
<tr>
<td>GER</td>
<td>6</td>
</tr>
</tbody>
</table>

Owayed AF et al, Arch Pediatr Adolesc Med, 2000
**Infant or Child with Recurrent Pneumonia**

- Often the clinician must make management decisions based on inconclusive information & the clinical scenario.
- GER related aspiration pneumonia may arise in the absence of esophagitis
- Normal esophageal pH monitoring does not exclude GER as a cause of aspiration pneumonia
- Combination of tests may aid Dx
  - BA lavage with LL Macrophages/pepsin
  - Nuclear scintigraphy
  - Swallowing assessment (VSS/FEES)

**PPI treatment of patients with GER and Neurodevelopmental delay**

- PPI therapy may be of benefit in some pediatric patients with esophagitis and recurrent pneumonia
- Double blind placebo controlled trials are needed in normal and neurologically abnormal children

**Does surgery change outcome?**

- Review of the Washington State CHARS database of pediatric hospital admissions
- Measured reported hospitalizations for “reflux related respiratory events” (RRE) including pneumonia, aspiration pneumonia, or mechanical ventilation in patients the year before and year after antireflux
- 1142 patients with antireflux surgery, 52% with events pre surgery.

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**Broncho-alveolar lavage?**

Lipid-Laden Macrophages

”Pepsin in BALF of children with chronic respiratory symptoms correlates positively with the number of proximal reflux events; however, it does not differentiate patients with reflux from those without”


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**Pepsin**

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Goldin, AB et al, Pediatrics 2006;118:2326

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Infant or Child with Recurrent Pneumonia

- No controlled studies demonstrate the benefits of any medical therapy
- The potential benefits of surgery are balanced with the recognition of potential complications.

Infant or Child with Asthma

- Symptoms of GER are common in children with asthma
- In a compilation of 13 case series- 61% of children with asthma had GER
- Of these, about 50% had no or minimal symptoms of GER (heartburn, vomiting)

Does GER cause asthma?

- Local axonal reflexes
- Neurokinines
- Edema
- Inflammation
- Bronchial hyperactivity
- GER
- Micro-aspiration
- Airway Vagal afferents
- Central Nervous System
- Vagal afferents

Does treatment with PPI improve asthma in adults?

- Double blind placebo controlled trial in 770 adults with moderate to severe persistent asthma
- Esomeprazole- 40 mg BID or placebo for 16wks
- No statistically significant improvement in the primary endpoint of morning peak expiratory flow (PEF) in treatment group vs placebo in the overall study population

Kiljander TO, Am J Respir Crit Care Med 2006;173:1091

Subgroup analysis showed that treatment decreased FEV1 only in patients with GER symptoms AND nocturnal asthma symptoms.

Does treatment with PPI improve asthma in children?

- No difference in asthma symptom scores at 12 wks (both groups decreased)
- Lung function studies and use of bronchodilators was similar in both groups.
- Quality of life survey showed improvement in Omeprazole group vs placebo group

pH probe studies performed in 165 children with asthma and GER symptoms
45 children had RI>5%
18 pts Omeprazole 20 mg od x 12 wks
18 pts Placebo

Stordal K et al, Arch Dis Child 2005;90:956
Infant or Child with Asthma

- In a patient with GER symptoms (heartburn and/or chest pain) and moderate to severe asthma a trial of PPI therapy is reasonable but efficacy may only be expected in patients with nocturnal asthma symptoms.
- Previous guidelines recommended pH probe to guide treatment decisions but evidence is lacking to support this recommendation.
- If treatment is initiated, outcome variables such as symptoms, medication use, PFT changes should be monitored.
- The role of both medical and surgical GERD therapy remains poorly defined.

Laryngeal Pharyngeal Reflux Disease (LPRD)

- Hoarseness
- Sore Throat
- Chronic cough
- Globus sensation

Laryngeal Findings in Adult “Normal” Volunteers

- High prevalence of GER changes in normal volunteers
  - Interarytenoid bar-70%
  - Arytenoid medial wall erythema- 29%
  - Posterior pharyngeal wall cobblestoning-21%
  - Intraarytenoid bar erythema-15%
  - Arytenoid medial wall granularity-13%
  - True vocal fold edema-10%
- Poor interobserver reliability

Esomeprazole Rx of Chronic Posterior Laryngitis in Adults

- Symptoms usually occur in the absence of classical symptoms of GER such as heartburn or chest pain.
- Upper endoscopy is often normal.
- pH probe is often normal.
- Laryngoscopic findings are the primary diagnostic criteria and are unreliable.
Esomeprazole Rx of Chronic Posterior Laryngitis in Adults
Vaezi MF et al, Laryngoscope 2006, 115:254

Infant or Child with Upper Airway Symptoms
• Several studies describe the presence of GER in children with either chronic or recurrent laryngeal symptoms
• Laryngoscopy is generally indicated to R/O other pathology but there is a lack of uniform interpretation of laryngeal findings for GER in children and adults
• Findings may be due to other etiologies such as allergy
• PPI therapy is of limited, if any value for all diagnosis except possibly chronic cough.

Conclusions
• Symptom based diagnosis is unreliable in children less than 8-12 years of age for the diagnosis GERD
• Endoscopic diagnosis requires findings of erosions
• Biopsy lack specificity for diagnosis of GERD in the absence of erosions
• A SHORT course of empiric acid suppression therapy may be reasonable in children with possible esophageal symptoms

Infant or Child with Upper Airway Symptoms
• The data available is inadequate to allow recommendations for Dx or Rx of possible GER related cough, hoarseness, stridor, vocal cord nodules or poor surgical healing in pediatric patients.
• Therefore, caution should be exercised in establishing acid reflux as the sole diagnosis in patients with chronic laryngeal symptoms
• Surgery should not be expected to improve symptoms in those patients that do not respond to PPI therapy

Conclusions
• Improvement following empiric acid suppression therapy does not confirm a diagnosis of GERD
• GERD may cause pneumonia but diagnostic approaches are unreliable
• GERD may exacerbate asthma but PPI therapy is potentially beneficial only in a small sub-group of patients