"Is GERD related to symptoms and diseases outside of the esophagus?"

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**Definitions**

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>GER</td>
<td>Passage of gastric contents into esophagus</td>
</tr>
<tr>
<td>GERD</td>
<td>Symptoms or complications that may occur when gastric contents reflux into esophagus or oropharynx</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>Passage of refluxed gastric contents into oral pharynx</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Expulsion of refluxed gastric contents from mouth</td>
</tr>
</tbody>
</table>

Vandenplas et al JPGN 49:498–547  2009

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**Prevalence of Regurgitation in Infancy**

- % of Infants
- Age (months)
  - 0-3
  - 4-6
  - 7-9
  - 10-12

- 1 time a day
- 4 times a day

Adapted from Nelson et al, Arch Pediatr Adolesc Med 1997;151:569

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Prevalence of GER Symptoms in Children


% of Children

Heartburn  Epigastric pain  Regurgitation  Heartburn and/or acid regurgitation

566 parents of children aged 3-9 yr  615 children aged 10-17 yr  2200 adults aged 25-74 years

The Antireflux Barrier

Esophagus  LES  Crural diaphragm  Intra-abdominal esophagus  Angle of His  Stomach

Transient LES Relaxations

Pharynx  UES  Esophagus  LES  Angle of His  Stomach

Tracings reprinted from Kawahara et al., Gastroenterology 1997;113:399
Esophageal Capacitance

- Shorter esophagus
- Smaller capacity

Gravity

Infant

Adult

Airway Protective Mechanisms

<table>
<thead>
<tr>
<th>ESOPHAGEAL DISTENTION</th>
<th>Small volume</th>
<th>UES contracts</th>
</tr>
</thead>
</table>

0.15 s

Vagal reflexes

Vocal cords close

Central apnea occurs

UES relaxes

0.3 s

Refluxate enters pharynx

0.6 s

Swallowing clears pharynx

1.0 s

Respiration resumes

Pathogenic Factors in GERD

Mechanisms of GERD

- 1
- 2

Mechanisms of Esophageal Complications

- Impaired esophageal clearance
- Defective tissue resistance
- Noxious composition of refluxate

Mechanisms of Airway Complications

- Vagal reflexes
- Impaired airway protection
Presenting Symptoms and Signs of GERD

- Recurrent vomiting in infant
- Recurrent vomiting and poor weight gain in infant
- Recurrent vomiting and irritability in infant
- Recurrent vomiting in older child
- Heartburn in child/adolescent
- Esophagitis
- Dysphagia or feeding refusal
- Apnea or ALTE
- Asthma
- Recurrent pneumonia
- Upper airway symptoms

Testing for GERD

- Is there a single test for GERD?
- What question does each test answer?
- How reproducible or reliable is the test?
- Does it guide our management and when is it useful?

Diagnostic approach in suspected GERD depends on presenting symptoms and signs

- History and physical examination
- Upper GI series
- Esophageal pH monitoring
- Esophagogastroduodenoscopy and biopsy
- Empirical medical therapy
Upper GI Radiography

**Advantage**
• Useful for detecting anatomic abnormalities

**Limitation**
• Cannot discriminate between physiologic and nonphysiologic GER episodes

Pyloric stenosis

Malrotation

Esophageal pH Monitoring

**Advantages**
• Detects episodes of reflux
• Determines temporal association between acid GER and symptoms
• Determines effectiveness of esophageal clearance mechanisms
• Assesses adequacy of H2RA or PPI dosage in unresponsive patients

**Limitations**
• Cannot detect nonacidic reflux
• Cannot detect GER complications associated with "normal" range of GER
• Not useful in detecting association between GER and apnea unless combined with other techniques
Physiologic Gastroesophageal Reflux (Mean upper limit of normal)

<table>
<thead>
<tr>
<th></th>
<th>Infants (N=509)</th>
<th>Children (N=48)</th>
<th>Adults (N=432)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of daily reflux episodes</td>
<td>73</td>
<td>25</td>
<td>45</td>
</tr>
<tr>
<td>No. of reflux episodes ≥ 5 min</td>
<td>9.7</td>
<td>6.8</td>
<td>3.2</td>
</tr>
<tr>
<td>Reflux index (% of time pH &lt; 4)</td>
<td>11.7%</td>
<td>5.4%</td>
<td>6%</td>
</tr>
</tbody>
</table>

Vandenplas et al JPGN 49:498–547 2009

Esophagogastroduodenoscopy (EGD)

Advantages
- Enables visualization and biopsy of esophageal epithelium
- Determines presence of esophagitis, other complications
- Discriminates between reflux and non-reflux esophagitis

Limitations
- Need for sedation or anesthesia
- Endoscopic grading systems not yet validated for pediatrics
- Poor correlation between endoscopic appearance and histopathology
- Generally not useful for extra-esophageal GERD

Multiple Intraluminal Electrical Impedance Measurement

Advantages
- Detects brief (<15 s) acidic GER episodes
- Useful for studying respiratory symptoms and GER in infants

Limitations
- Normal values in pediatric age groups not yet defined
- Analysis of tracings time-consuming
- Portable device unavailable for outpatient studies
Empiric Therapy

Diagnostic Workup

Presenting Symptoms and Signs of GERD

- Recurrent vomiting in infant
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Evaluation and Management of Dysphagia or Odynophagia

Infant
- GER not demonstrated to cause feeding difficulties
- Antireflux treatment not demonstrated to improve feeding
- Empiric therapy for GER not recommended
- If other symptoms suggest GERD → time-limited medical therapy

Older Child/Adolescent
- Barium esophagram to identify:
  - Anatomic abnormality
  - Motility disorder
- Upper endoscopy with biopsy
- Treatment without diagnostic evaluation not recommended

Sandifer Syndrome

Respiratory Symptoms of GER

- Apnea/ALTE
- Stridor and hoarseness
- Cough
- Wheezing
- Recurrent pneumonia

Mechanisms of Respiratory Responses to GER
Prevalence of Gastroesophageal Reflux in Children With Pulmonary Disease

% of Patients

Friedland et al, 1973
Berquist et al, 1981
Shapiro et al, 1979
Euler et al, 1979
Danus et al, 1976
Martin et al, 1982
Buts et al, 1986

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ALTE

Definition: Frightening episode in infant that is characterized by:
- apnea
- change in color
- change in muscle tone
- choking or gagging
and requires intervention by caretaker

Potential causes:
- Cardiac disorder
- Upper airway obstruction
- CNS disorder
- Infection
- GERD
- Intentional suffocation
GER and ALTE

• Recurrent regurgitation in 60% to 70% of infants with ALTE

• Abnormal esophageal pH studies in 40% to 80%

• Relationship between GER and obstructive or mixed apnea most convincing when infant was:
  – awake
  – supine
  – fed within past hour

Management of GER-Associated ALTE

• Esophageal pH monitoring is useful only if performed simultaneously with measurement of respiration and chest wall movement

• Infant is more likely to respond to antireflux therapy if:
  – emesis or regurgitation is present at time of ALTE
  – infant is awake
  – obstructive apnea is present

• Therapeutic options include:
  – thickened feedings
  – acid suppression

• Antireflux surgery is considered only in severe cases

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Does GER Cause Asthma?

GER → Asthma
GER ← Asthma
GER ⇄ Asthma
GER ≠ Asthma

Prevalence of GER in Infants and Children with Asthma

- GERD (abnormal esophageal pH studies) in 61% of infants and children with asthma
- GERD symptoms absent or mild in about 50% of those with persistent asthma and abnormal esophageal pH studies

N=668 pts in 13 case series

Effect of Antireflux Pharmacotherapy in Children with Asthma

Clinical improvement or reduced dosages of anti-asthmatic therapy in 63% of asthma patients with GERD treated with:

- Conservative management
- PPI treatment

N=168 pts in 4 case series
Asthma: When to Treat for GERD

<table>
<thead>
<tr>
<th>Persistent asthma and GER symptoms</th>
<th>Vigorous acid-suppressive therapy for 3 months, monitoring outcome variables</th>
</tr>
</thead>
</table>
| Persistent asthma and no GER symptoms | Consider esophageal pH monitoring or empiric treatment trial in children with:  
  - recurrent pneumonia  
  - nocturnal asthma > 1X weekly  
  - corticosteroid dependence  
  If pH studies positive → 3-month trial of antireflux medical therapy, monitoring outcome variables |

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Aspiration Syndromes

- Interstitial lung disease & pulmonary fibrosis
- Acid aspiration pneumonitis
- Aspiration pneumonia & pleural effusion
Aspiration From Swallowing or GER?

Lipid-Laden Macrophages

Aspiration From Swallowing or GER?

Barium Swallow
Technetium-99m Salivagram

Causes of Recurrent Pneumonia in Children

<table>
<thead>
<tr>
<th>Causes</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration</td>
<td>48 %</td>
</tr>
<tr>
<td>Immune disorder</td>
<td>10</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>9</td>
</tr>
<tr>
<td>Asthma</td>
<td>8</td>
</tr>
<tr>
<td>Respiratory tract anomaly</td>
<td>8</td>
</tr>
<tr>
<td>GER</td>
<td>5</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>12</td>
</tr>
</tbody>
</table>

N = 238 children hospitalized with pneumonia

Recurrent Pneumonia and GER

- GERD can cause recurrent pneumonia in absence of esophagitis
- Normal esophageal pH studies do not exclude GER as a cause
- Before considering GERD, rule out other causes
  - neuromuscular disease or esophageal or laryngeal anatomic abnormalities
- Incidence of GERD-related recurrent aspiration in otherwise healthy infants and children is rare

Management of Recurrent Pneumonia and GER

- Combination of tests may aid in diagnosis
  - flexible bronchoscopy with pulmonary lavage
  - nuclear scintigraphy
  - swallowing assessment (FEES)
- Severely impaired lung function → consider antireflux surgery
  - balance potential benefits with potential complications

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Evaluation and Management of GER-Related Laryngeal Symptoms

- Laryngoscopy generally indicated to rule out anatomic abnormalities of airway protection.
- Adult studies suggest that therapeutic trial must last >3 months to adequately assess efficacy.
- Treatment → association with GERD.

Possible Supraesophageal Complications of GERD

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental erosion?</td>
<td>Present in 20/37 children</td>
</tr>
<tr>
<td></td>
<td>Prevalence not increased in 53 with abnormal esophageal pH.</td>
</tr>
<tr>
<td>Recurrent sinus disease?</td>
<td>Improvement with antireflux treatment in 15/19</td>
</tr>
<tr>
<td></td>
<td>Prevalence similar in infants with and without GERD</td>
</tr>
<tr>
<td>Otitis media?</td>
<td>Otalgia improved with GERD therapy</td>
</tr>
<tr>
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<td>Prevalence not increased in children with GERD</td>
</tr>
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Treatment Options for Children and Adolescents

- Lifestyle changes
  - Dietary modifications
  - Altered sleep position
  - Weight reduction
  - Cigarette smoking cessation
- Pharmacotherapy
- Surgical therapy
### Conservative Therapy for GER

**For Infants**
- Normalize feeding volume and frequency
- Consider thickened formula
- Consider non-prone positioning during sleep
- Consider trial of hypoallergenic formula

**For Older Children**
- Avoid large meals
- Do not lie down immediately after eating
- Lose weight, if obese
- Avoid caffeine, chocolate, and spicy foods that provoke symptoms
- Eliminate exposure to tobacco smoke

### Pharmacotherapy

- Histamine-2 receptor antagonists
- Proton pump inhibitors

### Goals of Pharmacotherapy

- Control symptoms
- Promote healing
- Prevent complications
- Improve health-related quality of life
- Avoid adverse effects of treatment
Inhibition of Acid Secretion in Gastric Parietal Cell

PPIs in Adults With GERD
- Most potent inhibitors of acid secretion
- Pharmacologic studies
- Numerous randomized controlled trials
  - Superior to H2RAs in relieving reflux symptoms and healing esophagitis
  - Effective in patients unresponsive to high-dose H2RA
  - Superior to H2RAs in maintaining remission of esophagitis

Effect of Omeprazole on Esophagitis

Hassall et al, J Pediatr 2000;137:388
**PPI use in young children**

- **Chai G et al. Pediatrics 2012;130;23**
- **Van der Pol et al. Pediatrics 2011;127;925**

### Optimal Timing of PPI Dose

**Single PPI dose:**

**Administer 1 half-hour before breakfast**

**If second PPI dose:**

**Administer 1 half-hour before evening meal**

### Approaches to Acid-Reducing Therapy

**Step Down**
- Begin treatment with PPI
- Maintain improvement with PPI
- Switch to H2RA

**Step Up**
- Begin treatment with H2RA
- Inadequate response → PPI
- Inadequate response → ↑ PPI dose

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**TABLE 2: Top Drug Molecules Dispensed to 3–5 Months (N = 6.5 million prescriptions)**

<table>
<thead>
<tr>
<th>Drug Molecule</th>
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</tr>
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<tbody>
<tr>
<td>Amoxicillin</td>
<td>12.5</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>6.1</td>
</tr>
<tr>
<td>Jeotse</td>
<td>5.9</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>5.6</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>4.8</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>4.1</td>
</tr>
<tr>
<td>Amoxicillin/Budesonate</td>
<td>3.4</td>
</tr>
<tr>
<td>Domperidone/Budesonate/Delephosphine</td>
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**Shrm.**
Candidate for Antireflux Surgery in Childhood

Child Who:

- Fails medical therapy due to GERD
- Is dependent on aggressive or prolonged medical therapy
- Has persistent asthma or recurrent pneumonia due to GERD

Principles of Antireflux Surgery

- Restore intra-abdominal segment of esophagus
- Approximate diaphragmatic crurae
- Reduce hiatus hernia when present
- Wrap fundus around LES to reinforce antireflux barrier

Outcomes of Antireflux Surgery in Children

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success rate (complete relief of symptoms)</td>
<td>57 – 92%</td>
</tr>
<tr>
<td>Mortality related to operation</td>
<td>0 – 5%</td>
</tr>
<tr>
<td>Overall complication rate</td>
<td>2 – 45%</td>
</tr>
<tr>
<td>Dumping syndrome</td>
<td>NA</td>
</tr>
<tr>
<td>Gas bloat syndrome</td>
<td>2 – 8%</td>
</tr>
<tr>
<td>Small-bowel obstruction</td>
<td>1 – 11%</td>
</tr>
<tr>
<td>Wrap failure</td>
<td>1 – 13%</td>
</tr>
<tr>
<td>Reoperation rate</td>
<td>3 – 19%</td>
</tr>
</tbody>
</table>

NA = Not estimated; one report suggested < 30%.
Magnetic Device for Augmentation of the Lower Esophageal Sphincter.

Summary

• GER is common in healthy infants and usually resolves by 18 months of age
• Pediatric GER can present with variable symptoms
• Approach to diagnosis and treatment depends on presenting symptoms and signs
• Currently available tests often do not conclusively demonstrate a relationship between GER and specific symptoms
• Good history and clinical judgment are important for optimal evaluation and management