Gastro-esophageal reflux in children: a burning problem

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NASPGHAN-ESPGHAN Guidelines for Evaluation and Treatment of Gastro-Esophageal Reflux in Infants and Children

A Global, Evidence-Based Consensus on the Definition of Gastroesophageal Reflux Disease in the Pediatric Population
*Am J Gastroenterol* 2009;104:1278-95

Extraesophageal symptoms of gastroesophageal reflux disease (GERD) in children: a systematic review
V. Tolia, Y. Vandenplas
*Aliment Pharmacol Ther* 2009;29:258-72
A global evidence-based consensus on the definition of GERD in the pediatric population

GERD in pediatric patients is present when reflux of gastric contents is the cause of troublesome symptoms and/or complications

**Esophageal**

**Symptoms purported to be due to GERD**
- Infant or younger child (0–8 years), or older without cognitive ability to reliably report symptoms
- Excessive regurgitation
- Feeding refusal/anorexia
- Unexplained crying
- Choking/gagging/coughing
- Sleep disturbance
- Abdominal pain

**Symptomatic syndromes**
- Older child or adolescent with cognitive ability to reliably report symptoms
- Typical reflux syndrome

**Symptoms with esophageal injury**
- Reflux esophagitis
- Reflux stricture
- Barrett's esophagus
- Adenocarcinoma

**Definite associations**
- Sandifer's syndrome
- Dental erosion

**Possible associations**
- Bronchopulmonary
  - Asthma
  - Pulmonary fibrosis
  - Bronchopulmonary dysplasia
- Laryngotracheal and pharyngeal
  - Chronic cough
  - Chronic laryngitis
  - Hoarseness
  - Pharyngitis
- Rhinological and otological
  - Sinusitis
  - Serous otitis media

**Infants**
- Pathological apnea
- Bradycardia
- Apparent life-threatening events

*Where other causes have been ruled out (e.g., food allergy, especially in infants)***
GER is not associated with dental erosion in children.
Wild YK. Gastroenterology 2011;141:1605-11

cross-sectional study  59 children (9-17 y) with symptoms of GER
20 asymptomatic children (controls)

Controlling for age
dietary intake
oral hygiene,
there was no association between GER symptoms
and dental erosion by tooth location or affected surface.

Salivary flow did not correlate with GER symptoms or erosion.

Location-specific dental erosion is not associated with GER,
salivary flow, or bacterial load.
The “typical reflux syndrome…”

A. Does not exist in children
B. Cannot be diagnosed before the age of 8 years
C. Unconsolable crying in infants is the “infant manifestation” of the typical reflux syndrome
The “typical reflux syndrome…”

A. Does not exist in children
B. Cannot be diagnosed before the age of 8 years
C. Unconsolable crying in infants is the “infant manifestation” of the typical reflux syndrome
‘Typical Reflux Syndrome’ cannot be diagnosed in infants and children who lack the cognitive ability to reliably report symptoms.

Children < 8 (… up to 11) years old cannot report symptoms in a reliable / reproducible way.
The natural course of gastro-oesophageal reflux.
*Salvatore S. Acta Paediatr. 2004;93:1063-9*

<table>
<thead>
<tr>
<th>Symptoms/signs</th>
<th>Infants</th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>++++++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Heartburn</td>
<td>?</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>?</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Chest pain</td>
<td>?</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>?</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Excessive crying/irritability</td>
<td>+++</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Anaemia/melaena/haematemesis</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Food refusal/feeding disturbances/anorexia</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Failure to thrive</td>
<td>++</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Abnormal posturing/Sandifer’s syndrome</td>
<td>++</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Persisting hiccups</td>
<td>++</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Dental erosions/water brush</td>
<td>?</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hoarseness/globus pharyngeus</td>
<td>?</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Persistant cough/aspiration pneumonia</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Wheezing/laryngitis/ear problems</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Laryngomalacia/stridor/croup</td>
<td>+</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Chronic asthma/sinusitis</td>
<td>-</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Laryngostenosis/vocal nodules problems</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>ALTE/SIDS/apnoea/desaturation</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>+</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Sleeping disturbances</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Impaired quality of life</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Esophagitis</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Stenosis</td>
<td>-</td>
<td>(++)</td>
<td>+</td>
</tr>
<tr>
<td>Barrett’s/oesophageal adenocarcinoma</td>
<td>-</td>
<td>(++)</td>
<td>+</td>
</tr>
</tbody>
</table>

+++ very common; ++, common; +, possible; (+), rare; -, absent; ?, unknown.
GERD cases during 2000-05 The Health Improvement Network (THIN) UK primary care database via a computer search for diagnostic codes for GERD, followed by manual review of the patient records.

1700 children with a first diagnosis of GERD during 2000-05

Incidence GERD 0.84 / 1000 person-years

Incidence ↓ with age

from 1.48/1000 person-years among 1-year-old children until the age of 12 years,
whereupon it increased to a maximum at 16-17 years of 2.26/1000 person-years for girls
1.75/1000 person-years for boys. ….
In addition to typical GERD symptoms (epigastric pain, heartburn, reflux, regurgitation), 21.2% of children reported nausea or vomiting.

Children with neurological disorders were at increased risk of a GERD diagnosis.

Hiatus hernia and congenital esophageal disorders were also associated with a diagnosis of GERD.

Children and adolescents using antiepileptics, oral/inhaled steroids, beta-agonists and paracetamol had an increased risk of a GERD diagnosis.
Follow-up of a cohort of children and adolescents with GERD who were free of reflux esophagitis at initial diagnosis. 


The Health Improvement Network UK primary care database (which includes data on more than 2 million patients) to identify individuals aged 1-17 years with a first diagnosis of GER or heartburn in the period 2000-2005, via a computerized search followed by a manual review of the patient records.

⇒ 1242 individuals with an incident diagnosis of GERD but no record of esophagitis. This cohort was followed-up to detect new diagnoses of esophageal complications and extra-esophageal conditions.

⇒ During a mean follow-up period of almost 4 years, 40 children and adolescents had a confirmed new diagnosis of reflux esophagitis (incidence: 10.9/1000 person-years).

No cases of Barrett's esophagus, esophageal stricture or esophageal ulcer

Individuals with GERD had double the risk of an extra-esophageal condition such as asthma, pneumonia, cough or chest pain compared with children and adolescents with no diagnosis of GERD.
Pediatric GERD and acid-related conditions (ARC): trends in incidence of diagnosis and acid suppression therapy (1)


Cohorts of GERD/ARC children (age 0-18 years) were identified from a large US administrative claims database covering 1999-2005 using ICD-9 codes.

Comparison between various age and patient groups for incidence, healthcare utilization (HCU) costs, therapy discontinuation, and switching rates.

....
Pediatric GERD and acid-related conditions (ARC): trends in incidence of diagnosis and acid suppression therapy (2)


- Between 2000 and 2005, annual incidence of GERD/ARC diagnosis among infants (age ≤1 year) more than tripled (from 3.4 to 12.3%) and increased by 30% to 50% in other age groups.
- Patients diagnosed by GI specialists (9.2%) were more likely to be treated with PPIs compared to patients diagnosed by primary care physician (PCP).

<table>
<thead>
<tr>
<th>Year</th>
<th>PPI-Initiated</th>
<th>H²RA-Initiated</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td>31.5%</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>62.6%</td>
<td></td>
</tr>
</tbody>
</table>

PPI-initiated patients doubled when compared with H²RA-initiated patients:
- Associated with 30% less discontinuation
- 90% less therapy switching in 1st month
- Higher comorbidity burden
- Pre-treatment total HCU costs when diagnosed
Pediatric GERD and acid-related conditions (ARC): trends in incidence of diagnosis and acid suppression therapy (3)


Limitations:
- the use of an exploratory definition for GERD/ARC
- administrative claims data
- potential coding errors

⇒ The diagnosis of GERD/ARC incidence increased for children of all ages between 2000 and 2005.

Primare Care Physicians made the majority of diagnoses.

PPI initiations have surpassed H²RA initiations.
Prevalence and management of GERD in children and adolescents: a nationwide cross-sectional observational study.\(^{(1)}\)


Nationwide prevalence GERD in French children and adolescents 404 GP & 180 paediatricians (P): register of all children and adolescents (n = 10,394, 0-17 yrs, mean 3.8 ± 5.6 years; 5143 by GP and 5251 by P) who presented over two 3-day periods (14-16 and 26-28 May 2008).

For all children who, in the physician's opinion, showed symptoms of GOR, a 24-item questionnaire covering the history and management of GOR was completed.

Children with symptoms that impaired their daily lives were defined as having GERD, the remainder as having physiological GER.
15.1 % showed GER symptoms.

Extrapolation to French population:
prevalence GER 10.3 % -- GERD 6.2 %

There was a significantly (p < 0.05) greater use of volume reduction or milk thickeners and dorsal positioning among infants with GERD versus physiological GER.

Significantly (p < 0.05) more infants and children with GERD received pharmacological therapy.

PPI increased with age and was significantly (p < 0.05) higher among those with GERD.
Prevalence and management of GERD in children and adolescents: a nationwide cross-sectional observational study. (3)


<table>
<thead>
<tr>
<th>Prevalence of GER in France according to age</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-23 month</td>
</tr>
<tr>
<td>Extrapolation to French population</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GER symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-23 month</td>
</tr>
<tr>
<td><strong>Mean duration (month)</strong></td>
</tr>
<tr>
<td><strong>Typical symptoms</strong></td>
</tr>
<tr>
<td>Regurgitations</td>
</tr>
<tr>
<td>Vomiting</td>
</tr>
<tr>
<td>Crying</td>
</tr>
<tr>
<td>Heartburn</td>
</tr>
<tr>
<td><strong>Atypical symptoms</strong></td>
</tr>
<tr>
<td>Feeding difficulties, anorexia</td>
</tr>
<tr>
<td>Failure to thrive</td>
</tr>
<tr>
<td>Postural defects</td>
</tr>
<tr>
<td>Stridor</td>
</tr>
<tr>
<td>Chronic cough</td>
</tr>
<tr>
<td>Laryngitis, otitis</td>
</tr>
<tr>
<td>Asthma</td>
</tr>
<tr>
<td>Sinusitis</td>
</tr>
</tbody>
</table>

* The superscript letter signifies that the column value is significantly different (P<0.05) to the value of the presented column.
Prevalence and management of GERD in children and adolescents: a nationwide cross-sectional observational study. (4)

**Overall prevalence GER**
*In children 0 à 17 years*

**Prevalence GER-Disease**
*In children 0 à 17 years*

10.3% (1.4 million)  
6.2% (840,000)
Introduction   Symptoms Prevalence   Diagnosis   Treatment Conclusions
During in-vivo experiments, significant differences were found in acid exposure times derived from

- antimony: 4.0 +/- 0.8%
- ISFET: 5.7 +/- 1.1%
- glass pH electrodes: 9.0 +/- 1.7%
Impedance Scale

Low Conductivity = High impedance

Air

Esophageal Lining

Saliva

Food

Reflux

High Conductivity = Low impedance
1. Questionnaires  
   ⇒ 1\textsuperscript{st} to do, but…. limitations
2. Radiology  
   ⇒ anatomy
3. Scintigraphy
4. Ultrasound
5. Endoscopy (+ biopsy)  
   ⇒ ? Esophagitis
6. Manometry
7. pH metry  
   ⇒ ? acid GER-D in extra-esophageal symptoms
8. Impedance-metry  
   ⇒ ? acid & non-acid GER-disease
9. Therapeutic trial  
   ⇒ no data
Comparison of UGI contrast studies and pH/impedance tests for the diagnosis of childhood GER.


retrospective, compared UGI studies pH/impedance tests.

GER UGIS: 116 / 579 children (20%)
66 also underwent a pH/impedance test

Using pH/impedance tests as the reference for GER,

UGIS sensitivity of 42.8%
negative predictive value of 24%

No significant correlation (P > 0.05) between the reflux index
and the number of reflux episodes in the pH/impedance tests
and height of reflux in the UGI study
Detection of GER in children using combined MII and pH measurement: data from the German Pediatric Impedance Group.


Table I. Number of patients in the different subgroups with abnormal measurement data based on different pathological findings

<table>
<thead>
<tr>
<th></th>
<th>Patients with GI symptoms (n = 325)</th>
<th>Patients with pulmonary symptoms (n = 329)</th>
<th>Patients with neurologic symptoms (n = 46)</th>
<th>All patients (n = 700)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal measurements, n</td>
<td>114 (48 female, 66 male)</td>
<td>133 (57 female, 76 male)</td>
<td>23 (11 female, 12 male)</td>
<td>270 (116 female, 154 male)</td>
</tr>
<tr>
<td>Age, years, median (range)</td>
<td>6.5 (1 month-16 years)</td>
<td>2 (1 month-16 years)</td>
<td>0.5 (3 weeks-15 years)</td>
<td>2.8 (6 weeks-16 years)</td>
</tr>
<tr>
<td>Only pathological pH</td>
<td>26 (23%)</td>
<td>21 (16%)</td>
<td>2 (9%)</td>
<td>49 (18%)</td>
</tr>
<tr>
<td>Pathological MII and pH</td>
<td>55 (48%)</td>
<td>35 (26%)</td>
<td>11 (48%)</td>
<td>101 (37%)</td>
</tr>
<tr>
<td>Pathological MII</td>
<td>33 (29%)</td>
<td>77 (58%)</td>
<td>10 (43%)</td>
<td>120 (45%)</td>
</tr>
</tbody>
</table>
Cough and GER…

A. There is evidence that chronic cough is caused by GER
B. There is evidence that reflux may induce cough
C. There is evidence that PPI decrease cough
D. In patients with CF, mainly acid reflux is increased
Cough and GER…

A. There is evidence that chronic cough is caused by GER
B. There is evidence that reflux may induce cough
C. There is evidence that PPI decrease cough
D. In patients with CF, mainly acid reflux is increased
Esophageal impedance in children: symptom-based results
S. Salvatore J Pediatr 2010;157:949-54

Symptoms with associated reflux events

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Pts No.</th>
<th>Symptoms No.(median)</th>
<th>GER related No.(%)</th>
<th>AR related No.(%)</th>
<th>WAR related No. (%)</th>
<th>AlkR related No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crying</td>
<td>88</td>
<td>872 (8)</td>
<td>395 (45)</td>
<td>174 (44)</td>
<td>215 (54)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>48</td>
<td>229 (3)</td>
<td>196 (86)</td>
<td>80 (41)</td>
<td>103 (52)</td>
<td>13 (7)</td>
</tr>
<tr>
<td>Cough</td>
<td>102</td>
<td>975 (7)</td>
<td>510 (52)</td>
<td>243 (48)</td>
<td>247 (48)</td>
<td>20 (4)</td>
</tr>
<tr>
<td>Others</td>
<td>13</td>
<td>64 (3)</td>
<td>29 (45)</td>
<td>16 (55)</td>
<td>13 (45)</td>
<td>0</td>
</tr>
<tr>
<td>All</td>
<td>126</td>
<td>2172 (6)</td>
<td>1136 (52)</td>
<td>516 (45)</td>
<td>581 (51)</td>
<td>39 (3)</td>
</tr>
</tbody>
</table>
Esophageal impedance in children: symptom-based results
*S. Salvatore J Pediatr 2010;157:949-54*

Reflux episodes in relation with the 3 age groups and the 3 predominant symptoms.

<table>
<thead>
<tr>
<th>ITEM</th>
<th>CRYING</th>
<th></th>
<th></th>
<th>COUGH</th>
<th></th>
<th></th>
<th></th>
<th>VOMITING</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-6mo</td>
<td>6-12mo</td>
<td>&gt;12mo</td>
<td>1-6mo</td>
<td>6-12mo</td>
<td>&gt;12mo</td>
<td>1-6mo</td>
<td>6-12mo</td>
<td>&gt;12mo</td>
<td>1-6mo</td>
<td>6-12mo</td>
</tr>
<tr>
<td>No. patients</td>
<td>37</td>
<td>30</td>
<td>21</td>
<td>31</td>
<td>34</td>
<td>37</td>
<td>22</td>
<td>15</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. events</td>
<td>456</td>
<td>279</td>
<td>137</td>
<td>338</td>
<td>311</td>
<td>326</td>
<td>115</td>
<td>53</td>
<td>61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>11</td>
<td>6</td>
<td>5</td>
<td>9</td>
<td>7</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GER related (%)</td>
<td>44</td>
<td>44</td>
<td>50</td>
<td>56</td>
<td>58</td>
<td>43</td>
<td>90</td>
<td>87</td>
<td>75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AR associated (%)</td>
<td>36</td>
<td>57</td>
<td>43</td>
<td>29</td>
<td>60</td>
<td>57</td>
<td>20</td>
<td>52</td>
<td>76</td>
<td></td>
<td></td>
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<tr>
<td>WAR associated (%)</td>
<td>62</td>
<td>42</td>
<td>54</td>
<td>69</td>
<td>39</td>
<td>34</td>
<td>69</td>
<td>46</td>
<td>22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AlkR associated (%)</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>9</td>
<td>11</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Cow's milk challenge increases weakly acidic reflux in children with CMA and GERD.

*Borrelli O. J Pediatr 2012;161:476-481*

### Table II. Reflux characteristics during AAF and CM administration

<table>
<thead>
<tr>
<th></th>
<th>AAF period</th>
<th>CM period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of reflux episodes</td>
<td>65 (39-87.5)</td>
<td>105 (58-127.5)*</td>
</tr>
<tr>
<td>[median (25th to 75th)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemical composition of refluxate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[median (25th -75th)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acid episodes</td>
<td>31 (9.5-44)</td>
<td>34 (14-41)</td>
</tr>
<tr>
<td>Weakly acidic episodes</td>
<td>19 (13-26.5)</td>
<td>53 (38.5-60.5)*</td>
</tr>
<tr>
<td>Weakly alkaline episodes</td>
<td>5 (3.5-10)</td>
<td>10 (2.5-15)</td>
</tr>
<tr>
<td>pH-only reflux episodes</td>
<td>9 (7-16)</td>
<td>11 (5.5-15)</td>
</tr>
<tr>
<td>Reflux composition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liquid</td>
<td>71%</td>
<td>78%</td>
</tr>
<tr>
<td>Mixed</td>
<td>27%</td>
<td>21%</td>
</tr>
<tr>
<td>Gas</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Esophageal acid exposure time</td>
<td>3.4 ± 2.6</td>
<td>3.6 ± 2.7</td>
</tr>
<tr>
<td>(mean ± SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of long-lasting episodes (&gt;5 min) [median (25th -75th)]</td>
<td>3 (1-3)</td>
<td>2 (1.5-2.5)</td>
</tr>
</tbody>
</table>

*P < .001 by Wilcoxon signed rank test.

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**Figure 2.** Proportion of the type of reflux episodes during the 2 recording periods. Note the significant decrease in proportion of acid and pH-only reflux episodes, and the significant increase in the proportion of the weakly acidic reflux episodes. Data are expressed as percentage of the total number of reflux episodes.

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Related to allergy? Or faster gastric emptying AAF?
The relationship between GER and cough in children with chronic unexplained cough using combined impedance-pH-manometry recordings.


Both acid and WA GER may precede cough in children with unexplained cough, but cough does not induce GER. Objective cough recording improves symptom association analysis.
Although WA-GER is uncommon, acid GER is prevalent in children with CF. It is a primary phenomenon and is not secondary to cough.

One third of the children with CF have bile acids (BA) in saliva, which may indicate an increased risk for aspiration. However, the impact of salivary BA and potential aspiration on CF pulmonary disease needs further investigation.
45 children with chronic cough: 24-hour MII-pH
20 children with erosive reflux disease (ERD): controls.

24 children had
Cough-related reflux (CRR) in 24/45
(19 no GI symptoms)
Cough-unrelated reflux (CUR) in 21/45

CRR + ERD: ↑ AR, WAc, WAlk reflux
ERD: ↑ eso acid exposure & acid clearance time
than in CRR and CUR
CRR group  158 cough episodes related to reflux episodes
66% AR // 18% WAc // 16% Walk

17 children had positive SAP  7 for AR
5 for AR & WAc
4 for WAc & Walk
1 for WAlk.

In children with unexplained chronic cough,
asymptomatic acid and nonacid GER is a potential etiologic factor.
The increased acid exposure time and delayed acid clearance characteristic of ERD are absent in cough-related GER.
Nocturnal reflux in children and adolescents with persistent asthma and gastroesophageal reflux (1)

*Molle LD. J Asthma 2009;46:347-50*

38 patients 10 years (range 5 - 15) with persistent asthma for at least 2 years
GI symptoms: regurgitation, heartburn, and abdominal pain

GER: considered positive RI > 5%
Forced vital capacity (FVC), forced expiratory volume in 1 second (FEV(1)),
forced mid-expiratory flow rate (FEF(25-75%)), and FEV(1)/FVC ratio

GER prevalence was 47.3%.
RI supine 8.7% (3.2 to 23.6); upright 10.5% (5.2 to 15.0)
FEF(25-75%) was below the predicted value: 54.5% (39.4 to 96.9).
RI was not significantly correlated with FVC, FEV(1) and FEF(25-75%).
Nocturnal reflux in children and adolescents with persistent asthma and gastroesophageal reflux.


A high prevalence of GER was found in children and adolescents with persistent asthma, equally distributed in the supine (nocturnal) and upright positions.

There was no correlation with pulmonary function test.
The concept that infant irritability and sleep disturbances are manifestations of GER is largely extrapolated from adult descriptions of heartburn and sleep disturbances that improve with antacid therapy.

What is the evidence in infants?
Multicenter, DB, R, PC trial assessing the efficacy and safety of PPI lansoprazole in infants with symptoms of GER disease. 


Symptoms were tracked through daily diaries and weekly visits

**Efficacy:** > 50% reduction of feeding-related crying

216 infants screened, 162 randomized

<table>
<thead>
<tr>
<th>Treatment</th>
<th>44/81 (54%)</th>
<th>44/81 (54%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lansoprazole</td>
<td>responder</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>responder</td>
<td></td>
</tr>
</tbody>
</table>

No difference in any secondary measures or analyses of efficacy

<table>
<thead>
<tr>
<th>Event</th>
<th>Lansoprazole</th>
<th>Placebo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1 AEs</td>
<td>62%</td>
<td>46%</td>
<td>.058</td>
</tr>
<tr>
<td>Serious AEs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>lower RTI (n)</td>
<td>10</td>
<td>2</td>
<td>.032</td>
</tr>
</tbody>
</table>

**Conclusions**
Proton pump inhibitor use in pediatric patients less than 12 months of age
Chen IL. JPGN 2012;54:8-14.

Review by FDA
Prescription rate 2002-2009 in USA: x 11!

<table>
<thead>
<tr>
<th>Drug</th>
<th>Efficacy (PPI-placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>esomeprazole</td>
<td>0.69 (95% CI 0.35 – 1.35)</td>
</tr>
<tr>
<td>lansoprazole</td>
<td>1.00</td>
</tr>
<tr>
<td>pantoprazole</td>
<td>1.00</td>
</tr>
<tr>
<td>omeprazole</td>
<td>3 doses (0.5, 1.0, 1.5 mg/kg/day): NS</td>
</tr>
</tbody>
</table>

Introduction  Symptoms  Prevalence  Diagnosis  Treatment  Conclusions
Results: Of the 98 patients enrolled, 81 (82.7%) experienced symptom improvement determined by physician global assessment (PGA) during open-label esomeprazole treatment; 80 entered the double-blind phase. During this phase, discontinuation rates owing to symptom worsening were 48.8% (20/41) for placebo-treated versus 38.5% (15/39) for esomeprazole-treated patients (hazard ratio 0.69; \( P = 0.28 \)). Posthoc analysis of infants with symptomatic GERD (ie, no diagnostic procedure performed) revealed that time to discontinuation was significantly longer with esomeprazole than placebo (hazard ratio 0.24; \( P = 0.01 \); the complementary subgroup difference was not significant (hazard ratio 1.39; \( P = 0.48 \)). Esomeprazole was well tolerated.
PPI: side effects

- bacterial overgrowth
- *community-acquired pneumonia (children, adults)*
- *gastroenteritis (children)*
- candidemia (preterms)
- necrotizing enterocolitis (preterms)
- parietal cell hyperpalsia / benign gastric polyps
- case reports: acute interstitial nephritis, acute hepatitis
- osteopenia, hip fractures
- ? Allergy
- ? Magnesium

Chai G. Pediatrics 2012;130:23-31

### TABLE 3
Top Drug Molecules Dispensed to the Pediatric Population From US Retail Pharmacies According to Patient Age in 2010

<table>
<thead>
<tr>
<th>Drug Molecule</th>
<th>0–23 Months (N = 31.6 million prescriptions)</th>
<th>2–11 Years (N = 134.2 million prescriptions)</th>
<th>12–17 Years (N = 96.6 million prescriptions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Share, %</td>
<td>Drug Molecule</td>
<td>Share, %</td>
<td>Drug Molecule</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>17.3</td>
<td>Amoxicillin</td>
<td>11.3</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>6.1</td>
<td>Azithromycin</td>
<td>5.8</td>
</tr>
<tr>
<td>Nystatin</td>
<td>5.9</td>
<td>Albuterol</td>
<td>5.6</td>
</tr>
<tr>
<td>Albuterol</td>
<td>5.8</td>
<td>Montelukast</td>
<td>4.5</td>
</tr>
<tr>
<td>Cefdinir</td>
<td>4.9</td>
<td>Methylphenidate</td>
<td>3.9</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>4.2</td>
<td>Fluticasone</td>
<td>2.9</td>
</tr>
<tr>
<td>Amoxicillin/clavulanate</td>
<td>3.4</td>
<td>Prednisolone</td>
<td>2.7</td>
</tr>
<tr>
<td>Dextromethorphan/phenylephrine/</td>
<td>2.4</td>
<td>Cefdinir</td>
<td>2.6</td>
</tr>
<tr>
<td>chlorpheniramine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ramitidine</td>
<td>2.2</td>
<td>Cephalexin</td>
<td>2.3</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>2.0</td>
<td>Amoxicillin/clavulanate</td>
<td>2.2</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>1.8</td>
<td>Amphetamine/dextroamphetamine</td>
<td>2.0</td>
</tr>
<tr>
<td>Multivitamins with fluoride</td>
<td>1.7</td>
<td>Multivitamins with fluoride</td>
<td>1.7</td>
</tr>
<tr>
<td>Budesonide</td>
<td>1.6</td>
<td>Lisdexamfetamine</td>
<td>1.6</td>
</tr>
<tr>
<td>Lansoprazole*</td>
<td>1.6</td>
<td>Sodium fluoride</td>
<td>1.5</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>1.5</td>
<td>Ibuprofen</td>
<td>1.4</td>
</tr>
<tr>
<td>Mupirocin</td>
<td>1.4</td>
<td>Mometasone</td>
<td>1.4</td>
</tr>
<tr>
<td>Sulfamethoxazole/trimethoprim</td>
<td>1.3</td>
<td>Dexamethasone</td>
<td>1.4</td>
</tr>
<tr>
<td>Polymyxin b sulfate/tmp</td>
<td>1.0</td>
<td>Sulfamethoxazole/trimethoprim</td>
<td>1.2</td>
</tr>
<tr>
<td>Trimcinolone</td>
<td>1.0</td>
<td>Clonidine</td>
<td>1.1</td>
</tr>
<tr>
<td>Montelukast</td>
<td>0.9</td>
<td>Budesonide</td>
<td>1.1</td>
</tr>
<tr>
<td>All others</td>
<td>32.0</td>
<td>All others</td>
<td>41.8</td>
</tr>
</tbody>
</table>

Data include all formulations (eg, oral tablet, oral syrups, topical cream). Source: VONA, 2002 through 2010; extracted March 2011.

* A total of 515,000 lansoprazole prescriptions (358,000 prescriptions in patients aged 0 to <1 year and 157,000 prescriptions in patients aged 1 to <2 years).
## TOP 5 medications infants 0 – 1 year

<table>
<thead>
<tr>
<th>Medication group (ATC 3)</th>
<th>DDD</th>
<th>% DDD (**)</th>
<th>N° patients</th>
<th>RIZIV (in 10^6 €)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astma, inhalation (R03B)</td>
<td>4.242.010</td>
<td>45%</td>
<td>78.545</td>
<td>2,9</td>
</tr>
<tr>
<td>Sympathicomimetics inhalation (R03A)</td>
<td>983.727</td>
<td>11%</td>
<td>56.729</td>
<td>0,5</td>
</tr>
<tr>
<td>Betalactam-antibiotics, penicilline (J01C)</td>
<td>758.308</td>
<td>8%</td>
<td>94.809</td>
<td>0,8</td>
</tr>
<tr>
<td>PPI (A02B)</td>
<td>652.901</td>
<td>7%</td>
<td>14.484</td>
<td>0,3</td>
</tr>
<tr>
<td>Antimicrobials (S01A)</td>
<td>550.638</td>
<td>6%</td>
<td>27.292</td>
<td>0,1</td>
</tr>
</tbody>
</table>

2007: 120 663 births
2007: 14 484 infants treated with PPI/H2RA = 12%
Pediatric use of H2RA and PPI in Belgium (Inami/Riziv)

Daily Defined Dosis

<table>
<thead>
<tr>
<th>% Infants (0-1y) with Anti-Acid</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12.1</td>
<td>14.2</td>
<td>15.5</td>
<td>17.2</td>
<td>18.6</td>
</tr>
</tbody>
</table>


- Alginates/antacids and prokinetics ↓ with age (p<0.05)
- PPI ↑ with age (p<0.05)
Omeprazole and asthma outcome in children with asthma and GER-disease: a randomised control trial.
Stordal K. Arch Dis Child 2005;90:956-60

38 children (7-16 years): asthma and symptoms suggesting GERD and 24 hr pH metry RI > 5 %

Table 3  Outcome measures in children with asthma and GORD treated with omeprazole and placebo

<table>
<thead>
<tr>
<th></th>
<th>Omeprazole (n = 18)</th>
<th>Placebo (n = 18)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom score</td>
<td>-1.28 (-2.65 to 0.1)</td>
<td>-1.28 (-3.27 to 0.72)</td>
<td>1.00</td>
</tr>
<tr>
<td>PAQLQ</td>
<td>-0.62 (-0.29 to -0.95)</td>
<td>-0.50 (-0.29 to -0.70)</td>
<td>0.51</td>
</tr>
<tr>
<td>FEV_{1%} (mean, median)</td>
<td>-1.38 (0.33)</td>
<td>-2.01 (-0.50)</td>
<td>0.77</td>
</tr>
<tr>
<td>FEF_{25-75} (mean, median)</td>
<td>-0.07 (-0.05)</td>
<td>0.04 (0.05)</td>
<td>0.12</td>
</tr>
<tr>
<td>Rescue medication (mean, median)</td>
<td>-1.9 (0.0)</td>
<td>-1.9 (0.5)</td>
<td>0.89</td>
</tr>
<tr>
<td>ECP baseline</td>
<td>25.9 (14.3, 37.5)</td>
<td>20.2 (12.7 to 27.7)</td>
<td></td>
</tr>
<tr>
<td>ECP change</td>
<td>1.27 (-5.5 to 8.1)</td>
<td>1.39 (-4.3 to 7.1)</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Values expressed as changes from baseline (week 0) to end of treatment (week 12) with 95% confidence intervals for mean (± 1.96 SEM) unless otherwise stated.

NO effect
Lansoprazole (n:149)  
15 mg/d if weighing less than 30 kg  
30 mg/d if weighing 30 kg or more  

Placebo (n = 157).  
Mean age was 11 years (SD, 3 years)  

- Mean difference in change (lansoprazole minus placebo) in the Asthma Control Questionnaire score: 0.2 units (95% CI, 0.0-0.3 units).  
- No statistically significant difference in the mean difference in change for the secondary outcomes of  
  - forced expiratory volume in the first second (0.0 L; 95% CI, -0.1 to 0.1 L)  
  - asthma-related quality of life (-0.1; 95% CI, -0.3 to 0.1)  
  - rate of episodes of poor asthma control (RR 1.2; 95% CI, 0.9-1.5)
Lansoprazole for children with poorly controlled asthma: a RCT (2)
Writing Committee for the American Lung Association Asthma Clinical Research Centers. JAMA.2012;307:373-81

...  
115 children with pH metries: prevalence of GER was 43%
In the subgroup with a positive pH study,
no treatment effect for lansoprazole vs placebo
was observed for any asthma outcome.

Children treated with lansoprazole reported more respiratory infections
(relative risk, 1.3 [95% CI, 1.1-1.6]).
Patients with asthma and heartburn should be treated for the heartburn.

Despite a high frequency of abnormal reflux studies in asthmatic patients, only a select group with nocturnal asthma symptoms, or with steroid dependent, difficult to control asthma may benefit from long term medical or surgical anti-reflux therapy.
In this cohort study, 197,060 singletons born between 1996 and 2008 in northern Denmark were followed until the end of 2009. Data were obtained through Danish medical registries.

Asthma in offspring was defined as at least two prescriptions of both a β-agonist and an inhaled glucocorticoid and/or a hospital diagnosis of asthma during the follow-up.
Prenatal exposure to acid-suppressive drugs and the risk of childhood asthma: a population-based Danish cohort study (2)

Andersen AB. Aliment Pharmacol Ther. 2012;35:

...  

2238 (1.1%) children were prenatally exposed to PPIs and 24,506 (12.4%) children developed asthma during follow-up (median follow-up = 6.8 years).

The adjusted IRR of asthma associated with prenatal exposure to PPIs was 1.41 (95% CI: 1.27-1.56), compared with those unexposed.

The association did not vary by trimester of exposure.  

Prenatal exposure to H2RAs was associated with similar increase in risk.  

The aIRR for maternal PPI and H2RA use in the year after, but not during pregnancy was 1.32 (95% CI: 1.20-1.46) and 1.13 (0.93-1.36), respectively, compared with non-use during and in the year after pregnancy.
http://www.youtube.com/watch?v=5VzEMr4NhgE&feature=player_detailpage

http://www.youtube.com/watch?v=PvxTfGBszc8&feature=player_detailpage
A 14-day multicentre randomised double-blind double-dummy non-inferiority trial compared Gaviscon® (4 × 10 mL/day) and omeprazole (20 mg/day) in patients with 2-6 day heartburn episodes weekly without alarm signals.

The primary outcome was the mean time to onset of the first 24-h heartburn-free period after initial dosing. Secondary outcomes were the proportion of patients without heartburn by D7, pain relief by D7, and reduction in pain intensity by D7 and D14.

RESULTS:
278 patients were recruited; 120 were included in the Gaviscon® group and 121 in the omeprazole group for the per protocol no

CONCLUSION:
Gaviscon® was non-inferior to omeprazole in achieving a 24-h heartburn-free period...
Clinical study on the treatment of gastroesophageal reflux by acupuncture. Zhang CX,

Sixty patients with confirmed diagnosis of GER were randomly assigned to two groups. The 30 patients in the treatment group were treated with acupuncture, while the other 30 served as the control group. 

RESULTS:
Compared with those detected at T0, 24-h intraesophageal pH and bile reflux were significantly reduced in the treatment group.

CONCLUSION:
Acupuncture can effectively inhibit the intraesophageal acid and bile reflux in patients with GER.
The study is a prospective cohort study of mechanically ventilated pediatric patients. 

**RESULTS:**
All VAP patients had GER (50% alkaline reflux, 12.5% acidic reflux and 37.5% combined reflux).

**CONCLUSIONS:**
GER is a constant incident in mechanically ventilated pediatric patients, with...
Does gastroesophageal reflux scintigraphy correlate with clinical findings in children with chronic cough?

Bingol Boz A

A total of 72 children older than 7 years with chronic cough of unknown etiology were enrolled for this study. The scintigraphy was performed using a thallium-201 heart camera.

RESULTS:
Of 72 children, 65 children with a mean age of 10.3 +/- 2.3 (7-19) years had GER on gastroesophageal scintigraphy. Median reflux episodes were 3 (range 0-20).

CONCLUSION:
Scintigraphy should be used for the detection of GER in children who present with chronic cough.
59 patients (37 girls, 22 boys) aged 7-17 years (mean 14.7) with the symptoms of GER there were divided into 2 groups: subgroups

RESULTS:
The most common complain--in 16 (88.89%) patients was recurrent and/or chronic abdominal pain, next

CONCLUSIONS:
The clinical manifestation of duodenal reflux was very much alike as in acid gastroesophageal reflux in the examined group.
Five hundred cases diagnosed as gastroesophageal reflux disease were randomly divided into a combination group, an electroacupuncture group, and a Dalitong granule group.

RESULTS:
Compared with those before treatment, esophageal acid reflux, bile reflux, endoscopic score, and symptom score were decreased in all groups.

CONCLUSION:
Electroacupuncture and Dalitong granule can both inhibit esophageal acid reflux.
Large prescription databases (the IMS Vector One: National and Total Patient Tracker) were used to examine national drug util

RESULTS:
In 2010, a total of 263.6 million prescriptions were dispensed to the US pediatric population, 7% lower than in 2002, while prescriptions dispensed to the adult population increased 22% during the same time.

Analysis of pediatric drug utilization trends for the top 12 therapeutic areas in 2010 compared with 2002 showed decreases in systemic antibiotics (-14%), allergies (-14%), pain (-14%), depression (-5%), and cough/cold without expectorant (-42%) prescriptions, whereas asthma (14%), attention-deficit/hyperactivity disorder (46%), and contraceptive (93%) prescriptions increased. In 2010, amoxicillin was the most frequently dispensed prescription in infants.

CONCLUSIONS:
Changes in the patterns of pediatric drug utilization were observed from 2002 to 2010.
Role of nasopharyngeal reflux in the etiology of otitis media with effusion. Aydın E,

The study was performed in 20 children with OME and adenoid hypertrophy.

RESULTS:
In the study group, 25% (5 of 20) of the patients were found to have nasopharyngeal reflux.

CONCLUSIONS:
We detected higher nasopharyngeal and esophageal reflux rates in the OME group.
The association of obesity and asthma severity and control in children.
Quinto KB,

Even after adjusting for demographics, parental education level, asthma controller use, and gastroesophageal reflux disease.

CONCLUSIONS:
Our findings suggest that childhood obesity is associated with an increased risk of worse asthma control and exacerbations.
Impedance and extraesophageal manifestations of reflux in pediatrics.

Greifer M,

We retrospectively reviewed charts from patients who underwent MII-pH. Inclusion criteria were ages 0 to 21 years with extraesophageal symptoms. A total of 119 MII-pH studies were performed. Of those, 63 studies met inclusion criteria.

RESULTS:
No association was demonstrated between the extraesophageal signs and symptoms and pathological GER based on DeMeester score.
Several techniques have been used to diagnose gastroesophageal reflux (GER) in children. Savino A,
**US in the diagnosis of gastroesophageal reflux in children.**

Savino A,


### Table 1: Reported sonographic features of the normal gastroesophageal region

<table>
<thead>
<tr>
<th>Author and year</th>
<th>Intraabdominal esophageal length (mm)</th>
<th>Esophageal wall thickness (mm)</th>
<th>Esophageal diameter (mm)</th>
<th>His angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Meester et al. 1979 [45]</td>
<td>20-25</td>
<td>—</td>
<td>—</td>
<td>70-100°, normal, 100-130°, obtuse 130-180°, completely obtuse</td>
</tr>
<tr>
<td>Halkiewicz et al. 2000 [42]</td>
<td>17.6±5.2</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Esposito et al. 2001 [10]</td>
<td>From 18 in newborns to 34 in children&gt;6 years old</td>
<td>2.4-5.7</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Koumanidou et al. 2004 [2]</td>
<td>From 22.2 in neonates to 27.2 in infants 6-12 months old</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Fallahi et al. 2007 [28]</td>
<td>21.53±9</td>
<td>3.9±1.2</td>
<td>10.1±2.0</td>
<td>—</td>
</tr>
<tr>
<td>Hashemi et al. 2009 [43]</td>
<td>22.2±10.0</td>
<td>4.0±1.3</td>
<td>10.1±2.4</td>
<td>—</td>
</tr>
<tr>
<td>Dehdashti et al. 2010 [44]</td>
<td>22.0±1.8</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Karabulut et al. 2010 [46]</td>
<td>—</td>
<td>2.1±0.2</td>
<td>Proximal, 4.5±0.4</td>
<td>107.4±5.9 in male and 106.2±5.2 in female infants</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Distal, 8.5±0.6</td>
<td>—</td>
</tr>
</tbody>
</table>
Association between otitis media and gastroesophageal reflux: a systematic review.

Miura MS,

Studies with planned data collection, in children with chronic otitis media with effusion/recurrent acute otitis media, assess...

RESULTS:
Of 242 initial studies, 15 met inclusion criteria. The authors found a mean prevalence of gastroesophageal reflux disease in children with chronic otitis media with effusion/recurrent acute otitis media may be higher than the overall prevalence for children.

CONCLUSION:
The prevalence of gastroesophageal reflux disease in children with chronic otitis media with effusion/recurrent acute otitis media may be higher than the overall prevalence for children.

Presence of pepsin/pepsinogen in the middle ear could be related to physiologic reflux.

A cause-effect relationship between pepsin/pepsinogen in the middle ear and otitis media...
The objective of the present qualitative study was to develop the items and support the content validity for the Pediatric Quality of Life (PedsQL) gastrointestinal symptoms module.

**METHODS:**
The iterative process included multiphase qualitative methods. A literature review and patient and parent interviews were conducted to generate the items.

**RESULTS:**
Eleven domains were derived from the qualitative methods involving patient and parent interviews and expert opinion.

**CONCLUSIONS:**
Qualitative methods involving pediatric patients and their parents in the item generation process support the content validity of the PedsQL gastrointestinal symptoms module.
Oral manifestations of gastroesophageal reflux disease.
Ranjitkar S,

Numerous case-control and other studies involving confirmation of gastroesophageal reflux disease (GERD) by esophageal pH monitoring have demonstrated various oral manifestations of GERD. These include but are not limited to dental erosions, angular cheilitis, and anterior glossitis. The presence of these oral manifestations can be indicative of underlying GERD and serve as a useful diagnostic tool in the evaluation of patients with suspected reflux disease.
The effects and efficacy of antireflux surgery in children with gastroesophageal reflux

Mauritz FA,

In total, 17 eligible studies were identified, reporting on a total of 1,280 children.

CONCLUSION:
ARS in children shows a good overall success rate (median 86%) in terms of complete relief of symptoms.
Influence of percutaneous endoscopic gastrostomy on gastro-oesophageal reflux

Toporowska-Kowalska E

Fifteen children with neurological impairments (cerebral palsy, n=10; cerebroidolipofuscinosis, n=2; Aicardi syndrome, n=1)

RESULTS:
At baseline, GOR was detected in 6 of the 15 participants, and the second MII/pH session revealed GOR in 2 of the 15 children.

INTERPRETATION:
Identification of GOR based on MII/pH in children with neurological impairments...
**Esophageal impedance in children: symptom-based results**

*S. Salvatore J Pediatr (in press)*

---

**Reflux associated with symptoms according to age**

<table>
<thead>
<tr>
<th>Age group</th>
<th>Patients No.</th>
<th>Symptoms No.</th>
<th>Reflux-related No.</th>
<th>AR related No.</th>
<th>%</th>
<th>WAR related No.</th>
<th>%</th>
<th>AlkR related No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-6 mo</td>
<td>40</td>
<td>938</td>
<td>505</td>
<td>152</td>
<td>30</td>
<td>335</td>
<td>66</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>6-12 mo</td>
<td>36</td>
<td>649</td>
<td>354</td>
<td>204</td>
<td>58</td>
<td>145</td>
<td>41</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>&gt; 12 mo</td>
<td>50</td>
<td>575</td>
<td>276</td>
<td>160</td>
<td>58</td>
<td>100</td>
<td>36</td>
<td>16</td>
<td>6</td>
</tr>
</tbody>
</table>

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**Introduction**

**Symptoms Prevalence**

**Diagnosis**

**Treatment Conclusions**
Delayed gastric emptying rates and impaired antral motility in children fulfilling Rome III criteria for functional abdominal pain.

Devanarayana NM. Neurogastroenterol Motil 2012;24:420-5

102 children (4-14 years) fulfilling Rome III criteria for FAP
Age and sex compatible group of healthy children (n = 20)

<table>
<thead>
<tr>
<th></th>
<th>patients</th>
<th>controls</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Gastr Empt Rate</td>
<td>42.1%</td>
<td>66.2%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Amplitude antral contractions</td>
<td>56.5%</td>
<td>89%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Frequency contractions / 3 min</td>
<td>8.5</td>
<td>9.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Antral motility index</td>
<td>4.9</td>
<td>8.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Fasting antral area</td>
<td>1.4</td>
<td>0.6</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Gastric Emptying Rate negatively correlated with the scores obtained for severity of abdominal pain (r = -0.29, P = 0.004).
The impact of reflux burden on Pseudomonas positivity in children with cystic fibrosis.

Palm K

We reviewed the multichannel intraluminal impedance (pH-MII) tracings of 35 patients with CF between 2003 and 2010. We compared...

RESULTS:
The mean age was 13.5 ± 5.8 years. Twenty-seven patients (76%) were Pa positive.

CONCLUSIONS:
Increased reflux burden may predispose patients to Pa infection and worse lung function.
Ten pediatric 24-hour pH-impedance tracings were analyzed by 10 observers from 7 world groups.

**RESULTS:**
Overall, 1242 liquid and mixed GER events were detected, 490 (42%) were scored by the majority of observers, yielding moderate agreement.

**CONCLUSION:**
Interobserver agreement in combined pH-multichannel intraluminal impedance analysis in experts is moderate; only 42% of GER episodes were scored by the majority of observers.
Detection of gastroesophageal reflux in children using combined multichannel intraluminal impedance and pH measurement: data

Pilic D

The patients were divided into 3 symptom groups based on the main indication for the procedure.

RESULTS:
Overall, 270 measurements were abnormal: 101 (37%) showed abnormal

CONCLUSIONS:
From this large systematically standardized data collection of MII-pH me
Esomeprazole for the treatment of GERD in infants ages 1-11 months.
Esomeprazole for the treatment of GERD in infants ages 1-11 months.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Mean (SD) symptom score during open-label phase</th>
<th>Mean (SD) change from baseline in symptom score during double-blind phase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Screening, n = 84</td>
<td>Final week, n = 79</td>
</tr>
<tr>
<td>Vomiting/regurgitation</td>
<td>1.42 (0.76)</td>
<td>1.00 (0.72)</td>
</tr>
<tr>
<td>Irritability (crying/fussiness)</td>
<td>1.50 (0.67)</td>
<td>1.02 (0.74)</td>
</tr>
<tr>
<td>Feeding difficulties</td>
<td>1.16 (0.76)†</td>
<td>0.83 (0.76)†</td>
</tr>
<tr>
<td>Supræosophageal/respiratory disturbances (coughing, wheezing, labored breathing)</td>
<td>0.54 (0.69)</td>
<td>0.44 (0.69)</td>
</tr>
</tbody>
</table>

SD = standard deviation.
*Symptom severity: 0 = none; 1 = mild; 2 = moderate; 3 = severe.
† n = 83.
‡ n = 78.
Cow's milk challenge increases weakly acidic reflux in children with CMA and GERD.

Borrelli O. J Pediatr 2012;161:476-481

### Table III. Height of reflux episodes during AAF and CM administration

<table>
<thead>
<tr>
<th></th>
<th>CM period</th>
<th>AAF period</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total reflux episodes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>50 (24.5-61.5)</td>
<td>72 (47-94.5)*</td>
</tr>
<tr>
<td>Intermediate</td>
<td>6 (5-10)</td>
<td>10 (6.5-16)††</td>
</tr>
<tr>
<td>Distal</td>
<td>3 (0-3.5)</td>
<td>4 (3-6)††</td>
</tr>
<tr>
<td><strong>Acid reflux episodes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>25 (6-38)</td>
<td>25 (10-34)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>4 (3-7)</td>
<td>5 (2-7.5)</td>
</tr>
<tr>
<td>Distal</td>
<td>0 (0-2)</td>
<td>1 (0-2.5)</td>
</tr>
<tr>
<td><strong>Weakly acidic reflux episodes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>16 (12-20.5)</td>
<td>43 (33-51.5)*</td>
</tr>
<tr>
<td>Intermediate</td>
<td>2 (0.5-2)</td>
<td>3 (2-5.5)††</td>
</tr>
<tr>
<td>Distal</td>
<td>0 (0-2)</td>
<td>1 (0-3)††</td>
</tr>
<tr>
<td><strong>Weakly alkaline reflux episodes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>5 (0-10)</td>
<td>5 (0-10)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>0 (0-1)</td>
<td>0 (0-5)</td>
</tr>
<tr>
<td>Distal</td>
<td>0 (0-0)</td>
<td>0 (0-2)</td>
</tr>
</tbody>
</table>

Values given as median (25th-75th).

*P < .001 by Wilcoxon signed rank test.
†P < .01 by Wilcoxon signed rank test.
‡P < .05 by Wilcoxon signed rank test.
Cow's milk challenge increases weakly acidic reflux in children with CMA and GERD.

*Borrelli O. J Pediatr 2012;161:476-481*

17 (median age: 14 months) proven CMA + ? GERD

48-hour MII-pH monitoring
- first 24 hours: amino acid-based formula
- 2nd 24 hours: CM-based formula

Reflux episodes
- AAF (25-75th) CM (25-75th)
- Total: 65 (39-87.5) 105 (58-127.5) <0.01
- weakly acid: 19 (13-26.5) 53 (38.5-60.5) < .001

No differences in acid or weakly alkaline episodes