Discussing the Role of Reflux in Nasal and Sinus Disease: There is a Connection

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CRS – A Clinical Syndrome?

- Biofilm
- Bacterial Infection
- Congenital Factors
- Functional Factors
- Fungi
- Allergy
- Osteitis
- Supercurrent
- Reflux?

Conditions Associated with LPR

- chronic laryngitis
- vocal process granuloma
- subglottic stenosis
- asthma/reactive airway disease
- **chronic sinusitis**
- Lingual tonsil hypertrophy
- Eustachian tube dysfunction/SOM
- adenoid hypertrophy
- Zenker’s diverticulum
- laryngospasm
- laryngeal carcinoma
Relationship of Reflux Disease and Chronic Sinusitis

Theories

- Direct exposure of nasal mucosa to gastric acid, Pepsin (i.e. nasopharyngeal reflux)
  - Minimal acid exposure affects mucociliary function
  - Minimal defense mechanisms for gastric acid in respiratory mucosa

- Neurally mediated reflex inflammation of the nasal mucosa

- Role of H. pylori
Activity/ Stability of Human Pepsin: Implications for Reflux Attributed Laryngeal Disease

**Pepsin**
- Detectable levels in laryngeal epithelium after a reflux event
- Maximum activity at pH 2.0
- Inactive at pH 6.5 or higher
- Stable for at least 24 hours at pH 7.0
- Remains stable until pH 8.0
- Mechanism of injury - depletes carbonic anhydrase and breaks down intercellular jxns
Lingual Tonsil Hypertrophy and Proximal Pharyngeal Reflux

- Found a significant relationship between higher LTH grades and NP reflux (PH < 4 and pH < 5) and UES reflux.

Association of Nasopharyngeal and Laryngopharyngeal Reflux with Post-Nasal Drip Symptomatology


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Patients with PND symptomatology have a significantly higher incidence of reflux (based on pH study) into the nasopharynx and laryngopharynx.

Pharmacologic treatment of reflux is warranted in patients with PND complaints, especially those that lack objective findings of rhinosinusitis.
Evidence of a Connection Between Reflux and Sinusitis
Evidence for relationship of CRS and Reflux

- Chambers et al. (Laryngoscope 1997)
  - Retrospective review of 182 patients who had undergone ESS
  - History of GER was the only predictive factor of poor surgical outcome
    - Presence of heartburn or reflux symptoms requiring medication
  - Drawback of study
    - No pH studies or other diagnostic studies for reflux performed
Evidence for Relationship of CRS and Reflux

- Ulualp et al (AJR 1999)
- Found more reflux in CRS patients
- Greater incidence and number of pharyngeal acid reflux events
  - Medically refractory CRS- 7/11 (63%)
  - Controls- 2/11 (18%)
Evidence for relationship of CRS and Reflux

- DiBiase et al. (Annals of Int. Med. 1998)
- 18 patients with refractory CRS
  - 67% with improvement of sinus symptoms 5.8 months after initiation of medical or surgical treatment
  - No dramatic improvements

- Drawback
  - No control group
Evidence for relationship of CRS and Reflux

- DiBiase et al (Am J Gastroenterol 2002)
- Prospective study
- Abnormal pH studies
  - 9/11 (82%) CRS pts
- All CRS pts treated for 3 months with BID omeprazole with partial symptomatic improvement
Evidence for relationship of CRS and Reflux
Pediatric Population

- Bothwell et al (Oto-H&N, 1999)
- 28 patients who failed traditional medical therapy for CRS
- 89% of patients avoided ESS with medical treatment of GER
Is Gastric Reflux a Cause of OME in Children?


- Tasker et al. (Laryngoscope 2002)
- 59/65 MEEs with positive result for pepsin/pepsinogen (by antipepsin antibody)
  - Levels up to 1000x higher than serum levels
- Pepsin in MEE due to direct NP reflux of gastric contents
Nasal Pepsin Assay and pH Monitoring in CRS

Subjects
- 33 medically refractory CRS patients
- 20 controls without CRS

Each patient underwent:
- Dual monitor pH probe (UES)
  - LPR considered *any* reflux events at UES sensor
- Nasal lavage for pepsin assay
  - Not quantitative
Nasal Pepsin Assay and pH Monitoring in CRS

<table>
<thead>
<tr>
<th></th>
<th>CRS (n = 33)</th>
<th>Controls (n = 20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pharyngeal reflux events</td>
<td>29 (88%)</td>
<td>11 (55%)</td>
<td>.01</td>
</tr>
<tr>
<td>Nasal pepsin activity</td>
<td>27 (82%)</td>
<td>10 (50%)</td>
<td>.014</td>
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</tbody>
</table>

• All patients with positive pepsin assays had pharyngeal reflux events.

• Pepsin assays were negative in only 3 LPR patients

• Pepsin assay was 100% sensitive and 92.5% specific for detecting LPR
Conclusions

- Positive pepsin assay results correlated to pH study results
- Evaluation of pepsin in nasal lavage fluid may be used as a sensitive, noninvasive alternative test for LPR

Need better quantitative correlation of degree of reflux and pepsin assays (JD)
Direct Nasopharyngeal Reflux of Gastric Acid is a Contributing Factor in Refractory Chronic Rhinosinusitis

Laryngoscope, June 2005

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Objective of Study

- Determine if there is a difference in the amount of reflux between patients with persistent sinus symptoms and mucosal inflammation after ESS, compared to ESS successes and normal healthy volunteers.
## Subjects and Controls

<table>
<thead>
<tr>
<th>Study group</th>
<th>Previous ESS</th>
<th>Nasal mucosal inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study group</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Surgically refractory CRS (N=38)</td>
<td>Yes (&gt; one year postop)</td>
<td>no</td>
</tr>
<tr>
<td>Successful ESS controls (n=10)</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Non-CRS controls (n=19)</td>
<td>no</td>
<td>no</td>
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</table>
Probe placement by endoscopy
Abnormal Reflux Parameters

- **Nasopharynx**
  - 1 or more reflux events < pH 4 or 5

- **UES**
  - 7 or more events per 24 hour study
  - RAI ≥ 6.3
    
  (Vincent, et al)

- **Esophagus**
  - pH < 4 over 4% of study time
## Relationship of Reflux Disease and Chronic Sinusitis (Overall)

<table>
<thead>
<tr>
<th></th>
<th># with NP reflux pH&lt;4</th>
<th># with NP reflux pH&lt;5</th>
<th># with &gt;6.9 UES reflux episodes</th>
<th># with RAI &gt; 6.3</th>
<th># with esophageal reflux &gt;4% of study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CRS patients</strong> (n=38)</td>
<td>15 (39%)</td>
<td>29 (76%)</td>
<td>28 (74%)</td>
<td>22 (58%)</td>
<td>25 (66%)</td>
</tr>
<tr>
<td><strong>Control group</strong> (n=29)</td>
<td>2 (7%)</td>
<td>7 (24%)</td>
<td>11 (38%)</td>
<td>6 (21%)</td>
<td>9 (31%)</td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>.004</td>
<td>.00003</td>
<td>.006</td>
<td>.007</td>
<td>.007</td>
</tr>
</tbody>
</table>
Conclusions

- Compared to controls, patients with medically/ surgically refractory CRS have a significantly greater incidence of:
  - NPR episodes below pH 4 and 5
  - UES RAI and # of reflux episodes
  - GER
  - Higher reflux, SNOT-20, SSS, and exam scores
Conclusions

- There is a significant percentage of CRS patients with NPR as a contributing factor
  - pH <5 is critical factor in the NP

- Maximal medical treatment of surgically refractory CRS should include treatment of LPR/NPR
Conclusions

- There is good evidence in the literature that:
  - Reflux is found in a higher proportion of CRS patients compared to controls
  - There is evidence for NP reflux and nasal reflux of gastric contents in CRS patients
    - Confirmed by pH studies and pepsin assay
- Reflux likely is a contributing factor to CRS in a subset of patients
  - Children
  - Surgically refractory CRS patients
- Causation not proven
Conclusions
Recommendations for Treatment

- Treat LPR in CRS patients with
  - Reflux symptoms or signs
    - Lingual tonsil hypertrophy
  - Post-nasal drip
  - Refractory sinus disease
- Weigh risk of treatment of LPR
  - Increased risk of hip fracture
THANK YOU FOR YOUR ATTENTION