The Link Between Rhinosinusitis and Asthma

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### History of The Relationship Between Upper and Lower Airway Disease

<table>
<thead>
<tr>
<th>Event</th>
<th>Description</th>
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<tbody>
<tr>
<td>Galen (200 AD)</td>
<td>Purged the nostrils of secretions to relieve the lungs</td>
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<tr>
<td>Kratchner (1870)</td>
<td>Stimulating feline upper airways (SO₂, ether) increased pulmonary resistance</td>
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<td>Voltolini (1871)</td>
<td>Asthma improved with polypectomy</td>
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<td>Dixon (1903)</td>
<td>Electrical stimulation of nose caused bronchoconstriction in cats</td>
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<td>Sluder (1919)</td>
<td>Eight asthmatics worsened with irritation of the sphenopalatine ganglion; cocaine reversed it</td>
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<tr>
<td>History (cont)</td>
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<tr>
<td><strong>• Gottlieb (1925)</strong></td>
<td>– 31 of 117 patients with asthma had sinusitis</td>
</tr>
<tr>
<td><strong>• Weille, Chobot (1930s)</strong></td>
<td>– 72% with sinusitis</td>
</tr>
<tr>
<td><strong>• Berman, Rachelefsky, Schwartz, Zimmerman (1970s)</strong></td>
<td>– Up to 53% with sinusitis</td>
</tr>
<tr>
<td><strong>• Slavin (1980s)</strong></td>
<td>– Sinus surgery improved asthma</td>
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</table>
The Link Between Rhinosinusitis and Asthma

• Epidemiologic observations
• Physiologic observations
• Clinical observations
Demographics - Rhinitis

- 75% to 95% of individuals with asthma have rhinitis
- Approximately 25% of individuals with rhinitis have asthma
- 75% of sinusitis have concomitant rhinitis
  - 65% allergic rhinitis
  - 25% nonallergic rhinopathy

Demographics - Rhinosinusitis

- More than two thirds of individuals with severe asthma have sinusitis
  - Up to 100% in some studies
  - Severe asthma > mild-moderate asthma
- 53% to 75% of children with asthma have abnormal sinus x-rays
- Cannot predict if sinusitis will be found on CT scan by sinus-related symptoms
- About 25-35% of sinusitis patients have asthma vs. 5% in normals
Thus, rhinosinusitis is found far more frequently in asthma than might be expected if they were coincidental diseases. And, asthma is far more frequent in patients with sinusitis then expected. These observations suggests a close and pathogenically related association.
Nasal polyps and asthma

• Nasal polyps are found in about 7% of asthmatics
  – 13% of nonallergic asthmatics
  – 10-15% of adult onset asthmatics

• 30% of nasal polyp patients have asthma

• Half the patients with polyps + asthma patients have AERD

• Of AERD patients, >70% have polyps
What are the mechanisms by which sinusitis affects asthma?
Putative Pathogenetic Mechanisms

• Postnasal drip seeding lungs
  – Not supported by most studies

• Systemic absorption of mediators
  – Illogical, not supported by studies

• Nasal obstruction - Loss of nasal filter
  – Might explain rhinitis- asthma connection
  – Not related to sinusitis
Putative Pathogenic Mechanisms

- Autonomic nervous system abnormalities
  - $\beta$-adrenergic hyporeactivity
  - Cholinergic and $\alpha$-adrenergic hyperreactivity
    - Proven for rhinitis and asthma, but not studied in sinusitis
Putative Pathogenetic Mechanisms:

• Continuous mucous membranes with contiguous disease
  – United airways disease
  – Infectious versus allergic-inflammatory
  – Chronic sinusitis is chronic and indolent, like asthma
  • Both are eosinophil-rich, associated with increased secretions
  – Probably distinct but quite similar diseases
Putative Pathogenic Mechanisms

- Sinus mucosal inflammation
- Sino-Naso-Bronchial reflex
- Sinus sensory nerves cause increased cholinergic efferent output to airways
- Increased cholinergic reactivity
  - Muscle contraction, vascular leak, mucus secretion, edema formation, mediator release
  - Enhanced eosinophil attraction and secretion
- Fits both physiologic and clinical observations
Ultrastructure of Airway Epithelium

Trachea and large bronchi. Ciliated and goblet cells predominant, with some serous cells and occasional brush cells, undifferentiated (intermediate) cells, and Clara cells. Numerous basal cells and occasional Kulchitsky cells present.

Bronchioles. Epithelium (lower). Ciliated cells dominant and Clara cells progressively increase distally along airways. Goblet cells and serous cells decrease distally and are absent in terminal bronchioles. Occasional undifferentiated and brush cells may be present. Basal cells and especially Kulchitsky cells are uncommon in distal airways.
## Origin of Nasal Reflexes

<table>
<thead>
<tr>
<th>Reflexes arising from the nose</th>
<th>Reflexes arising elsewhere</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasosinobronchial</td>
<td>Posture/recumbent</td>
</tr>
<tr>
<td>Sneeze</td>
<td>Crutch</td>
</tr>
<tr>
<td>Nasonasal</td>
<td>Exercise</td>
</tr>
<tr>
<td>Nasopharyngeal</td>
<td>Cold</td>
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<tr>
<td>Nasosalivary</td>
<td>Gustatory rhinitis</td>
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</tbody>
</table>
Gustatory Rhinitis: Effect of Atropine on Total Protein Secretion

Gustatory Rhinitis

- Caused by sensory stimulation of mouth and pharynx
- Mediated by sensory reflexes to the nose
- Stimulates cholinergic and sensory nerve stimulated glandular secretion
- Treated by anti-cholinergics or capsaicin desensitization
Gustatory Rhinitis

- In practice:
  - Older individuals
  - Males = females
  - Co-morbid with nonallergic rhinopathy
  - Any food, not just hot or spicy
  - Treated with ipratropium nasal spray
    - 1-2 sprays 5-10 min pre-prandial
Relevant Clinical Observations

• Acute sinusitis often precipitates acute asthma
• Management of chronic rhinosinusitis improves asthma management
  Both medical and surgical management
• In many (most) severe asthmatics, asthma cannot be well-managed unless sinusitis is also controlled
Clinical observations

• Peters Study: Sinusitis and Asthma in Adults, 64 subjects with asthma, 62 controls
  – CT of sinus on presentation to ED (scored)
  – 19/64 subjects with asthma (2/62 controls), extensive sinusitis
  – Only 2/64 subjects with asthma (28/62 controls) with no disease

The Effect of Medical Treatment of Sinusitis on Asthma

- Businco 1981
- Cummings 1983
- Rachelefsky 1984
- Friedman 1984
- McNally 1997
- Ragab 2006

All reported improvement in asthma
# Studies of the Effect of Sinus Surgery on Asthma (Pre-FESS)

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>% Improved</th>
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<tbody>
<tr>
<td>Weille</td>
<td>1936</td>
<td>100</td>
<td>56</td>
</tr>
<tr>
<td>Davison</td>
<td>1969</td>
<td>24</td>
<td>23</td>
</tr>
<tr>
<td>Slavin</td>
<td>1982</td>
<td>33</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Werth</td>
<td>1984</td>
<td>22</td>
<td>22</td>
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</tbody>
</table>

FESS = functional endoscopic sinus surgery.
Studies Showing Improvement of Asthma After FESS

• Children

• Adults
My Experience

• Most CRS can be well-managed medically
• Good medical management of sinusitis (and polyps) is critical to asthma management
• I send *very* few sinusitis patients to surgery
  – Usually only refractory polyp patients
• Think that proper FESS helps some patients in the long term management of refractory, complicated sinusitis and in some but not all asthmatics
Conclusion

- Epidemiologic, physiologic, and clinical observations support a strong link between rhinosinusitis and asthma.
- The mechanism responsible for the link has not been clarified, but neural reflexes appear to be important – sino-nasal-bronchial reflex.
- Evidence supports aggressive upper airway therapy as an important adjunctive treatment in the care of the patient with asthma.