AIRWAY NEURAL CONTROL IN ASTHMA AND COPD

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NIH Guidelines for the Diagnosis and Management of Asthma

Definition of Asthma:
“Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role … In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment. The inflammation also causes an associated increase in the existing bronchial hyperresponsiveness to a variety of stimuli.”
NIH Guidelines for the Diagnosis and Management of Asthma

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The Nervous System Plays an Essential Role in the Pathogenesis of Asthma and COPD.

NERVES

- Chest Tightness
- Airways Hyperresponsiveness
- Cough
- Reversible Airways Obstruction
- Airway Smooth Muscle Contraction
- Mucus Secretion
- Control of Vascular Tone
- Dyspnea
**Reversible Airways Obstruction in Asthma is Largely Dependent Upon Cholinergic Nerves.**

(25 patients studied)

(Modified from Ruffin et al. 1977)
Reversible Airways Obstruction in COPD is Dependent Upon Cholinergic Nerves.

(Modified from Tashkin et al. 1986)
Airways Hyperresponsiveness in Asthma is Largely Dependent Upon Cholinergic Nerves.

<table>
<thead>
<tr>
<th>Provocation</th>
<th>Effect</th>
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<tbody>
<tr>
<td>Beta blockers</td>
<td>Abolished response</td>
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<tr>
<td>Bradykinin</td>
<td>5-fold increase in PD&lt;sub&gt;35&lt;/sub&gt;</td>
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<tr>
<td>Capsaicin</td>
<td>60% reduction in response</td>
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<tr>
<td>Distilled water</td>
<td>50–100% reduction in response</td>
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<tr>
<td>Exercise</td>
<td>30% reduction in response</td>
</tr>
<tr>
<td>Histamine</td>
<td>10-fold increase in PC&lt;sub&gt;100&lt;/sub&gt; SRaw</td>
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<tr>
<td>Hyperpnea</td>
<td>Abolished response in children</td>
</tr>
<tr>
<td>Prostaglandin D&lt;sub&gt;2&lt;/sub&gt;</td>
<td>12- to 22-fold increase in PC&lt;sub&gt;20&lt;/sub&gt;</td>
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<tr>
<td>Psychogenic stimulation</td>
<td>Abolished response</td>
</tr>
<tr>
<td>Reflux or esophageal acidification</td>
<td>Abolished response</td>
</tr>
<tr>
<td>Thromboxane A&lt;sub&gt;2&lt;/sub&gt;</td>
<td>23-fold increase in PC&lt;sub&gt;20&lt;/sub&gt;</td>
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(from Canning et al., 2012)
Inhaled Drugs for Asthma and COPD Will Only Work in the Airways that are Accessible to Aerosols.

The Nervous System Plays an Essential Role in the Pathogenesis of Asthma and COPD.

Anticholinergics are NOT universal nerve blockers/neuromodulators
Extrinsic Vagal Innervation of the Human Airways

- Trachea
- Right bronchus
- Left bronchus
- Right vagus nerve
- Upper lobe bronchus
- Middle lobe bronchus
- Lower lobe bronchus
- Not connected
Hypoxia-induced Airway Narrowing: Increased in Asthmatics and Absent in Lung Transplant Patients

from Molino et al., 1993
Extreme Dyspnea from Unilateral Pulmonary Venous Obstruction

Demonstration of a Vagal Mechanism and Relief by Right Vagotony

SCOTT F. DAVIES, KENNETH R. MCQUAID, CONRAD IBER, CHARLES D. MCARTHUR, MICHAEL J. PATH, DAVID S. BEEBE, and HOVALD K. HELSETH

[Graphs showing respiratory rate, ventilation, and end-tidal PCO₂ across different workloads for Vagus Intact and Vagus Interrupted conditions, with data points and error bars indicating mean ± 2SD for ventilations, respiratory rate, and end-tidal PCO₂. Range for inspiratory time is also shown.

AM REV RESPIR DIS 1987; 136:184-188]
Loss and then Restoration of the Cough Reflex in Lung Transplant Patients

Mechanical Stimulation

Chemical Stimulation

from Duarte et al., 2008
Thank you