SMALL AIRWAYS DISEASE: ASTHMA & COPD

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Richard W. Weber, M.D. Disclosures

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– Genentech

SMALL AIRWAYS INFLAMMATION IN ASTHMA & COPD

• In healthy lungs, small airway resistance accounts for ~10% of the total resistance
• In asthma & COPD small airway resistance accounts for ~50% of total resistance
The disease process in asthma is located in all parts of the bronchial tree, including small and large airways.

Asthma Disease Site

van den Berge M et al. Chest 2011;139:412-423

Small airway walls thickened in severe asthma

Courtesy Sally Wenzel
Pattern of inflammatory cells also differs by lung region

Different distribution of inflammatory cells: Mast cells

Courtesy Sally Wenzel
Inflammation of Small Airways in Asthma
Q Hamid et al. J Allergy Clin Immunol 1997;100:44-51

Surgical lung specimens from 6 patients with asthma and 10 controls were examined. There was a similar inflammatory process present in the peripheral (<2mm diameter) compared with the central airways.

ASSESSMENT OF SMALL AIRWAYS

- Forced spirometry
  - FVC, FEV1, FEV1/FVC (FEV1%)  
  - FEF50, FEF25-75
- Forced oscillation technique
  - Resistance
  - Reactance
- Nitrogen washout
  - Single-breath (closing volume)
  - Multiple-breath (Scond & Sacin)
- Imaging
  - HRCT
  - Micro-CT
- Exhaled nitric oxide (FENO)
Pulmonary Function Tests

- PEFR (effort dependent, not for diagnosis, PFM dependent)
- FEV1 (usual measure of lung function)
- FEV1/FVC (reflects obstruction)
- TLC (essential for Dx of hyperinflation or restriction)
- DLCO (for emphysema, interstitial lung diseases)
- FEF25-75 (over-sensitive measure of obstruction)
ASSESSMENT OF SMALL AIRWAYS
**FE_{NO}** identifies persistent eosinophilia in severe asthma


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**Figure Caption:**

**A** and **B**: The change in asthma control after treatment with ICSL correlates with changes in SABA scores (McNemar test: I, P < 0.01; II, P < 0.001) and changes in forced volume: I, P < 0.01; II, P < 0.001.

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**Figure Caption:**

**D**: Peripheral Resistance (PEEP)

Healthy, MildMed, Severe, COPD.
TREATMENT DIRECTED TO THE SMALL AIRWAYS

- Oral Therapy
  - Oral corticosteroids
  - Theophylline
  - Oral beta adrenergic agonists
  - Leukotriene modifiers

- Inhaled corticosteroids
  - MDI versus DPI
  - Ultrafine particle MDI

Table 5 Spearman’s correlation for IOS parameters and spirometry

<table>
<thead>
<tr>
<th>Spirometry as % predicted</th>
<th>FEV₁</th>
<th>FVC</th>
<th>FEF_{25-75}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total resistance (R5)</td>
<td>−0.57**</td>
<td>−0.57**</td>
<td>−0.60**</td>
</tr>
<tr>
<td>Peripheral resistance (R5−R20)</td>
<td>−0.69**</td>
<td>−0.61**</td>
<td>−0.71**</td>
</tr>
<tr>
<td>Central resistance (R20)</td>
<td>−0.15</td>
<td>−0.25*</td>
<td>−0.15</td>
</tr>
<tr>
<td>Reactance (X5)</td>
<td>−0.65**</td>
<td>−0.68**</td>
<td>−0.60**</td>
</tr>
<tr>
<td>Resonant frequency (RF)</td>
<td>−0.67**</td>
<td>−0.62**</td>
<td>−0.68**</td>
</tr>
</tbody>
</table>

* P < 0.05; ** P < 0.001
INHALED CORTICOSTEROID PARTICLE SIZE

- Beclomethasone-HFA
- Beclomethasone-HFA/Formoterol
- Ciclesonide-HFA
- Flunisolide-HFA
- Fluticasone-HFA 2.4 μm
- Mometasone-HFA 3.7 μm


Data on file, Teva Respiratory, LLC; 2010.

The relationship of particle size (MMAD) and better lung deposition to clinical efficacy is unknown.
Lung Deposition of QVAR (beclomethasone dipropionate HFA) Inhalation Aerosol vs Advair

The clinical efficacy of better lung deposition is unknown.
Results based on an open-label, nonrandomized study of 7 male patients; the images shown are from 1 patient.

van den Berge M et al. Chest 2011;139:412-423

Oropharyngeal & Lung Deposition

van den Berge M et al. Chest 2011;139:412-423

Response to small-particle ICS

FIG 5. Eosinophils before and after hydrofluoroalkane-flunisolide in peripheral and central airways. Values are presented as means ± SEMs. *P < .001 versus pretreatment. Adapted from Hauber et al.40