Physiology of the Small Airways

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Questions

1) Is the physiology of a small airway different?
2) and Why should I care?
What is a SMALL Airway?

"Silent Lung Zone"

Structure has Consequences

Paleophysiology

- Weibel A: In: Foundations Of Lung Disease

- Green M: St Thomas Hosp Gazette 62:136 1964

Control of Airway Caliber & Patency

Smooth Muscle
Nerves
Structure
VOLUME

Figure 1. Calculated total resistance of each generation plotted against generation number.

Green M. St. Thomas Hosp Gazette 62:136 1964

Figure 2. Airways resistance of lungs from animals of varying ages. The control and experimental groups were paired equalled. Although there appears to be a reduction in resistance occurring in all ages, the peripheral resistance value appears much less at above age 5. This is thought to be due to the length of the peripheral airways increase more than relative weight during the first four years of life. But later, these increase very slowly.

Mechanisms of Airway Obstruction

Normal
Narrowing
Closure
Oclusion
Obliteration

Peripheral Airways

Normal subject  Asthmatic subject

Narrowing of Parallel Airways

\[ R = \frac{8nl}{\pi r^4} \]
And Now for a Little Circuit Theory

Series: \[ R_1 \parallel R_2 \parallel R_3 = \frac{R_1 + R_2 + R_3}{3} \]

Parallel: \[ R_1 \parallel R_2 \parallel R_3 = \frac{R_1 R_2 R_3}{R_1 R_2 + R_2 R_3 + R_1 R_3} \]

Obstruction of Parallel Airways

So obstruction is better than narrowing!

Large and small airways in asthma

Normal, Central, Peripheral
How do we assess small airways in living people?


Intrabronchial Pressure Measurement


Paleophysiology

Measurement of Peripheral Resistance (Rp) or collateral ventilation

Mützer. In: The Lung 1997
Peripheral Airway Resistance

![Graph showing flow resistance (Pb) vs. flow (ml/min) for asthmatics (90%) and normals (103%).]

Wagner, ARRD 151:548 1990

The Signal is the Noise

![Graph showing challenge (cool, dry at high flow ≤ 5 min) and response (Rp).]

Kaminsky et al, AJRCCM 152:1784 1995

The rise in Rp is correlated AHR

![Graph showing Rp (cm H2O/ml/min) for control, non-Nocturnal Asthma, and Nocturnal Asthma.]

Kraft et al, AJRCCM 163: 1551 2001
Assessment of The Small Airways

- Frequency Dependence Mechanics
- Closing volume
- FEV1 and FVC
- Residual Volume
- Imaging Techniques

Criteria for Small Airway

- RL ~ normal
- PV ~ normal
- Freq dependant C or R

Frequency Dependence of Compliance

Criteria for Small Airway

- RL ~ normal
- PV ~ normal
- Freq dependant C or R

Closing Volume/Capacity

![Graph showing closing volume/capacity for unstable and stable asthma]

Unstable asthma
Stable asthma

Percent Predicted

FEV1, TLC, FRC, RV, RV/TLC, CV/VC, CC/TLC

p = .02
p = .03

Small airways function and exacerbation rate in asthma

![Graph showing relationship between small airways function and exacerbation rate in asthma]

Controlled for patient age and years of follow-up.

p = .005

Exacerbation rate/year
Lung attenuation & asthma control

Mitsunobu et al, ERJ 2003

Images courtesy of the Center for In-vivo Hyperpolarized Gas MR Imaging, University of Virginia.
The structural basis of airways hyperresponsiveness in asthma


Brochodilator Response is Airway Opening

Hyperinflation Defends the FEV₁
Changes in Lung Function on Montelukast

<table>
<thead>
<tr>
<th>Variable</th>
<th>Measurement</th>
<th>Effect Size</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁ liters</td>
<td>0.16 ± 0.06</td>
<td>p &lt; 0.01</td>
<td></td>
</tr>
<tr>
<td>FVC liters</td>
<td>0.18 ± 0.07</td>
<td>p &lt; 0.01</td>
<td></td>
</tr>
<tr>
<td>TLC liters</td>
<td>+0.06 ± 0.05</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Vₕg liters</td>
<td>-0.13 ± 0.05</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>RV liters</td>
<td>-0.13 ± 0.06</td>
<td>p &lt; 0.05*</td>
<td></td>
</tr>
<tr>
<td>Rₕg (mmHg/Lps)</td>
<td>-1.39 ± 0.74</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

Am Chest tightness correlates with RV

r (Spearman): 0.20 (p = 0.41)
r (Spearman): 0.55 (p = 0.04)
**Small Airways Assessment**

**Circa 1969**
- RL within normal limits
- Normal PV curve
- Frequency dependence of CL

**Circa 2012**
- FEV1 and FVC are decreased
- FEV1/FVC ratio ~ normal
- TLC is normal or high
- RV is high
- Closing volume ±

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**Control of Airway Caliber & Patency**

- Smooth Muscle
- Nerves
- Structure
- VOLUME

- Smooth Muscle
  - Luminal contents
  - mucus
  - liquid
  - fibrin
  - surfactant
- SHEER NUMBER

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**Why Should I Care about the Small Airways**

1. Small airways contribute to the severity and phenotype of asthma
2. Small airways disease determines both AHR and symptoms
3. Effects of Ultrafine medications may be due to selective action on the small airways
4. It needs to be established whether and which small airway tests can be used to predict clinical course and to guide targeted therapy
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