



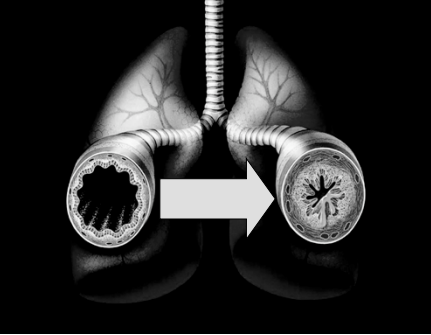
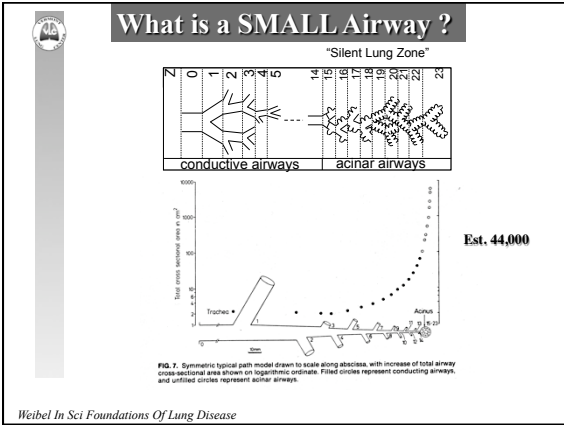
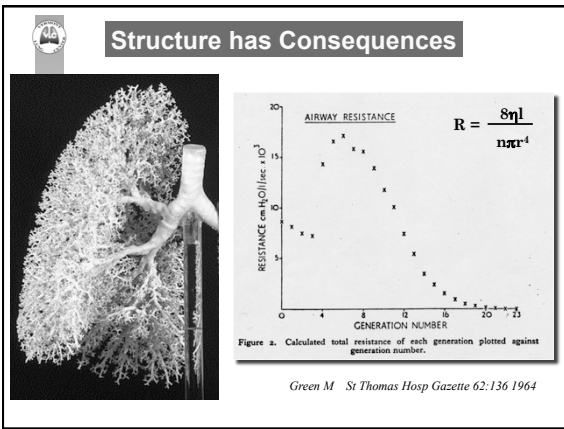

**Physiology
of the
Small Airways**
Charlie Irvin PhD
Vermont Lung Center
University of Vermont

 The image cannot be displayed. Your
WAO Cancun, Mexico
December, 2011

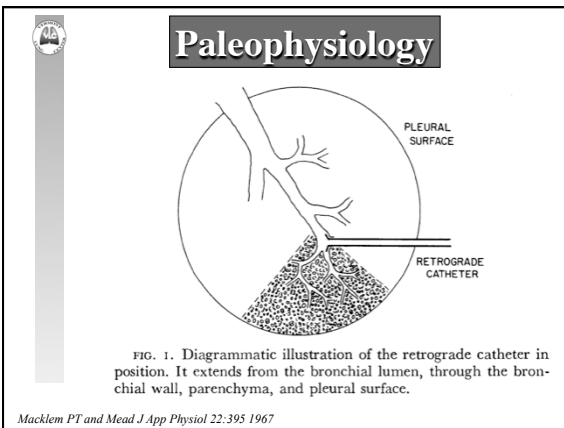

Questions

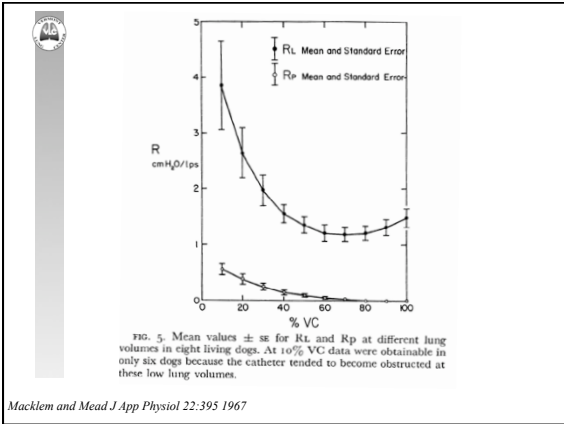
1) Is the physiology of a
small airway different?
2) and Why should I care?

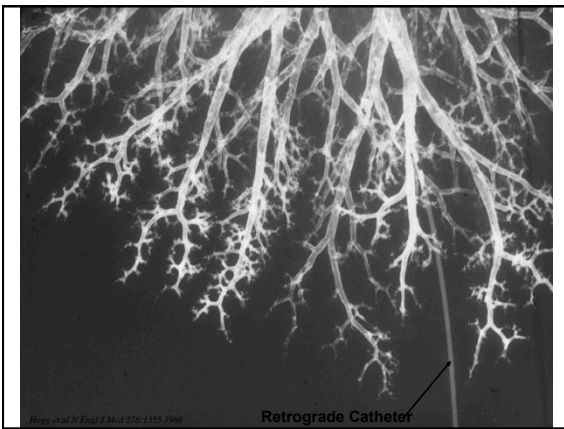

Pathophysiology of Asthma
Common Wisdom


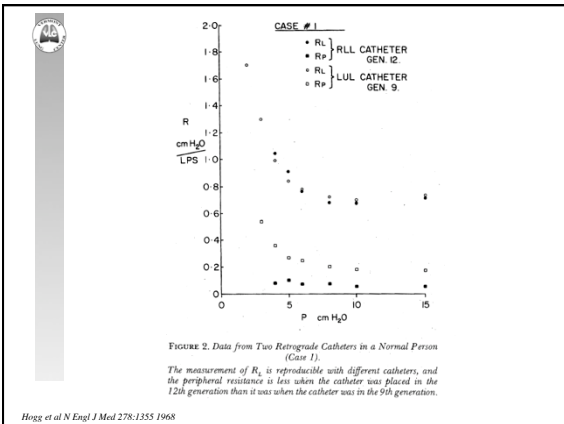


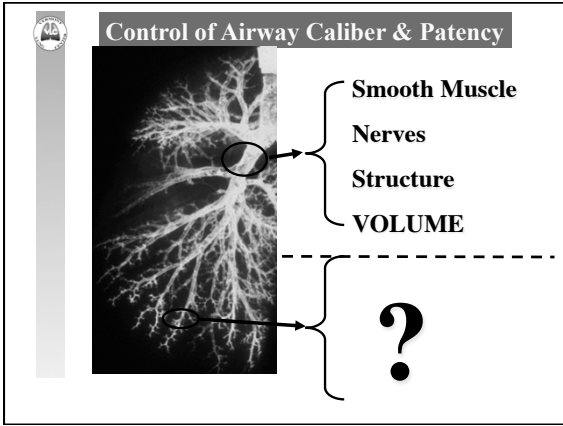


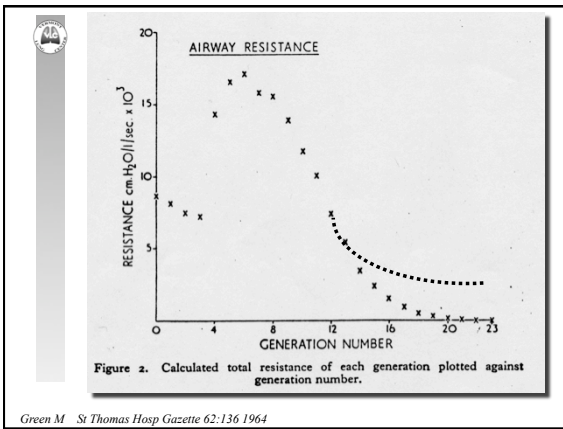




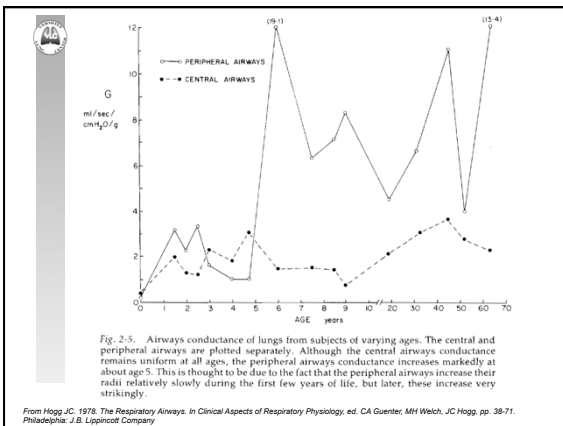








Green M. *St Thomas Hosp Gazette* 62:136 1964



Mechanisms of Airway Obstruction

Normal Narrowing Closure Occlusion Obliteration

Bosse et al Ann Rev Physiol 72:437 2010

Peripheral Airways

Normal subject **Asthmatic subject**

Narrowing of Parallel Airways

16 Fold ↑

$$R = \frac{8\eta l}{\pi r^4}$$

And Now for a Little Circuit Theory

Series: $R_1 + R_2 + R_3 = R_{eq}$

Parallel: $R_{eq} = (1/R_1 + 1/R_2 + 1/R_3)^{-1}$

Obstruction of Parallel Airways

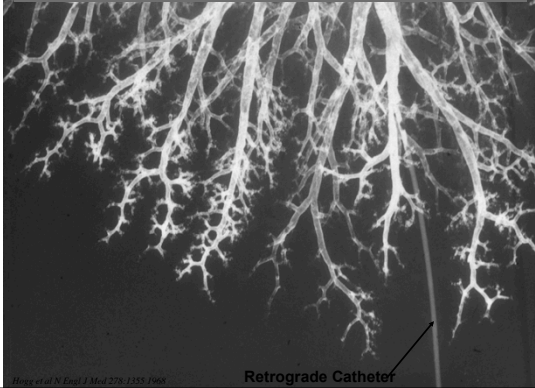
So obstruction is better than narrowing!

Large and small airways in asthma

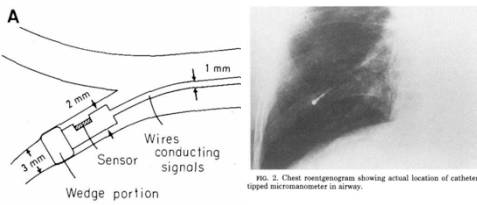
	Normal	asthma	
			Central
			Peripheral

Mauad, Bel, Sterk. J Allergy Clin Immunol 2007;120:997-1009

How do we assess small airways in living people?



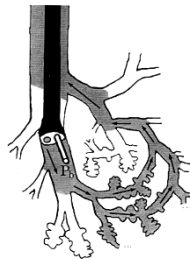
Intrabronchial Pressure Measurement



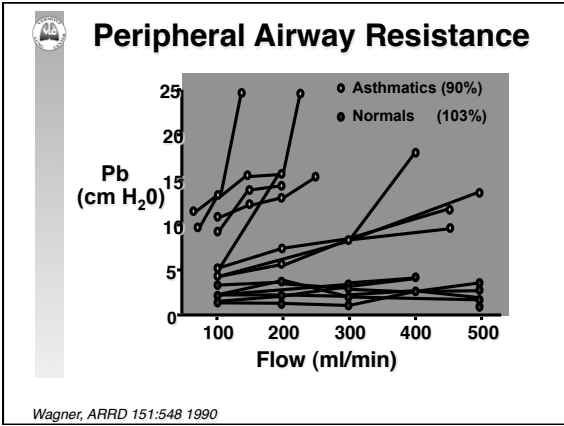
Yanai et al J Appl Physiol 72:1016 1992

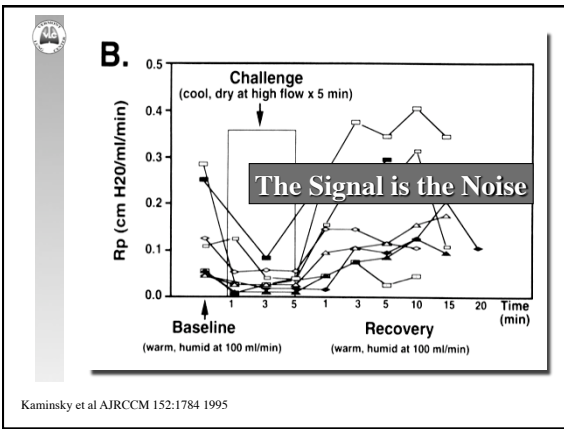
Paleophysiology

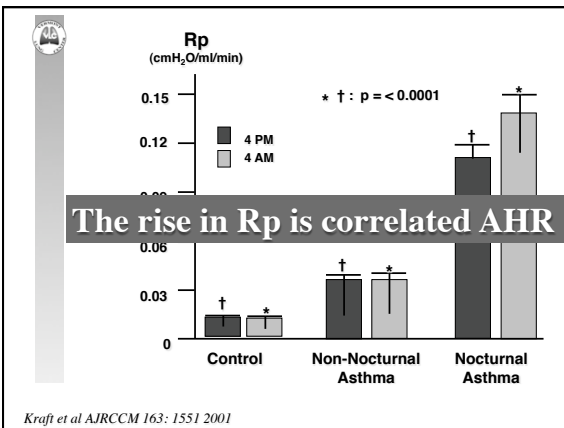
Measurement of Peripheral Resistance (R_p) or collateral ventilation



Mitzner. In: The Lung 1997



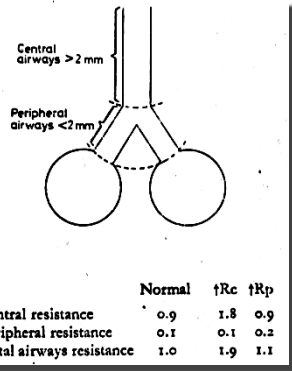






Assessment of The Small Airways

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



P T Macklem



Frequency Dependence of Compliance

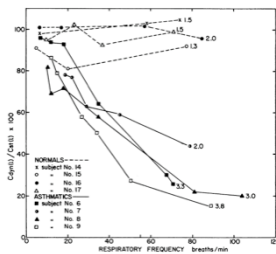
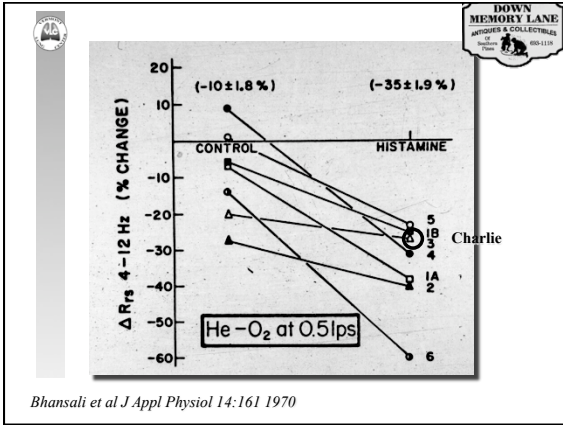


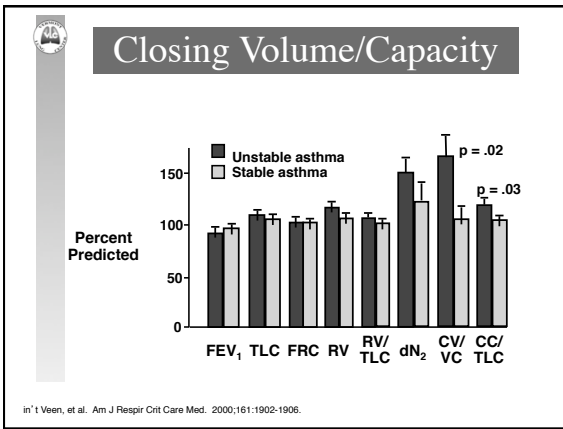
FIGURE 3 $C_{v(t)}$ as a percentage of $C_{v(0)}$ at different frequencies in four asthmatic subjects (—) and four normal subjects (---) of similar age. The number at the right of each graph is the value obtained for R_c at the time of the study.

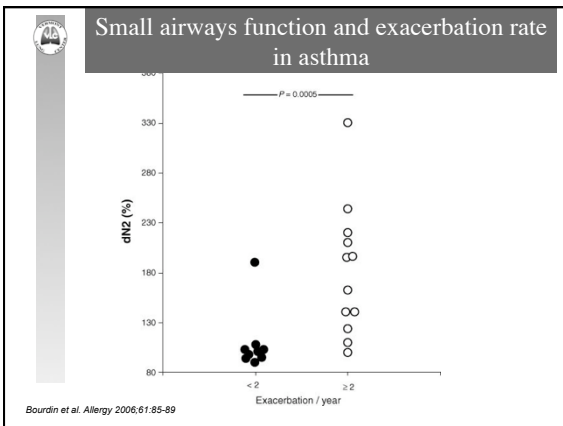
Criteria for Small Airway

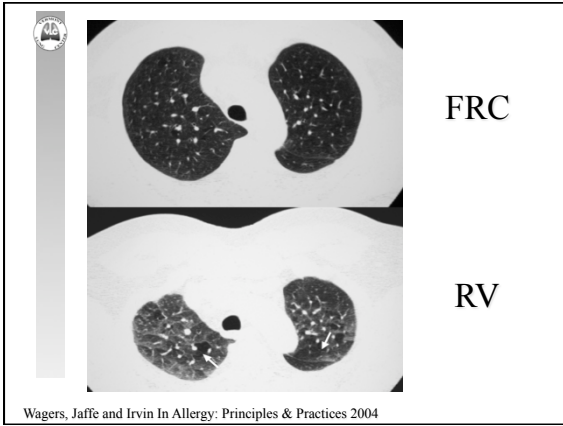
- RL ~ normal
- PV ~ normal
- Freq dependant C or R

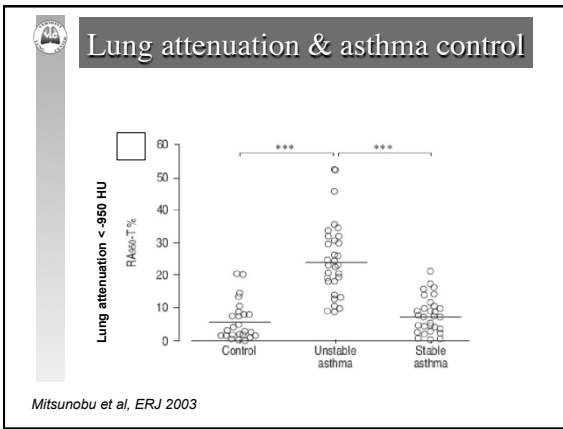
Woolcock et al J Clin Invest 48:1097 1969















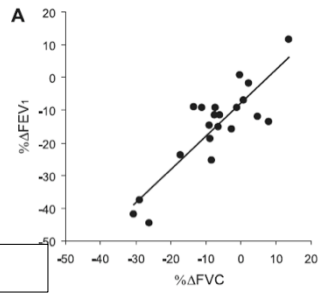
The structural basis of airways hyperresponsiveness in asthma

Robert H. Brown,^{1,2,3} David B. Pearce,³ George Pyrgos,³
Mark C. Liu,^{3,4} Alkis Togias,^{3,4} and Solbert Permutt³
¹Department of Anesthesiology and Critical Care Medicine, ²Department of Environmental Health Sciences,
³Division of Physiology, Department of Medicine, ⁴Division of Pulmonary and Critical Care Medicine and
⁵Division of Allergy and Clinical Immunology, The Johns Hopkins Medical Institutions, Baltimore, Maryland
Submitted 19 September 2005; accepted in final form 1 February 2006



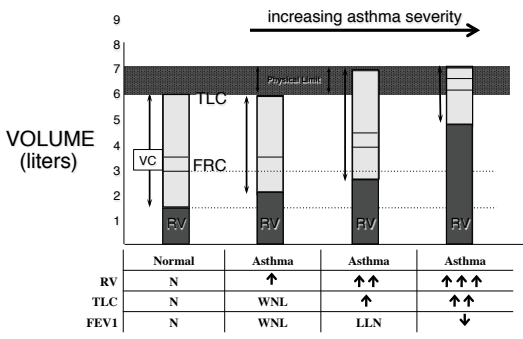


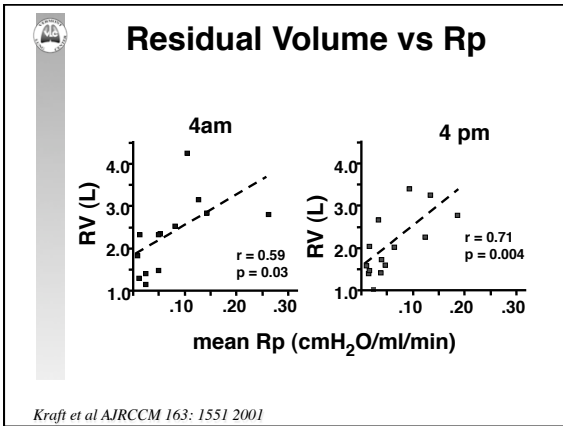
Brochodilator Response is Airway Opening



Brown et al J Appl Physiol 101:30 2006

Hyperinflation Defends the FEV₁

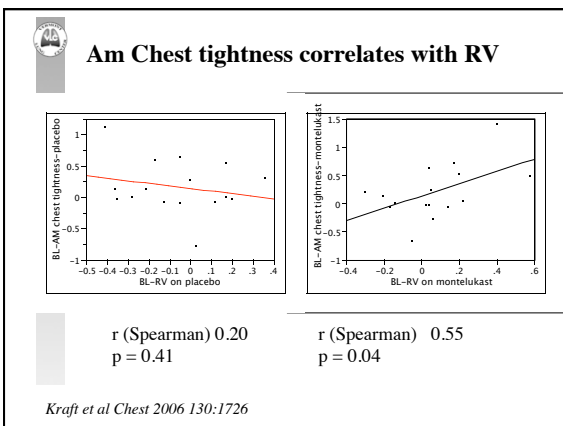




Changes in Lung Function on Montelukast

FEV ₁ liters	0.16 ± 0.06	p < 0.01
FVC liters	0.18 ± 0.07	p < 0.01
TLC liters	+0.06 ± 0.05	NS
V _{Ig} liters	-0.13 ± 0.05	NS
RV liters	-0.13 ± 0.06	p < 0.05*
R _{US} (cmH ₂ O/lps)	-1.39 ± 0.74	NS

Kraft et al Chest 2006 130:1726



Small Airways Assessment

<u>Circa 1969</u>	<u>Circa 2012</u>
• RL within normal limits	• FEV1 and FVC are decreased
• Normal PV curve	• FEV1/FVC ratio ~ normal
• Frequency dependence of CL	• TLC is normal or high
	• And RV is high
	• Closing volume \pm

Control of Airway Caliber & Patency

Smooth Muscle
Nerves
Structure
VOLUME

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

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