

# Airway Remodeling in Asthma (and COPD)

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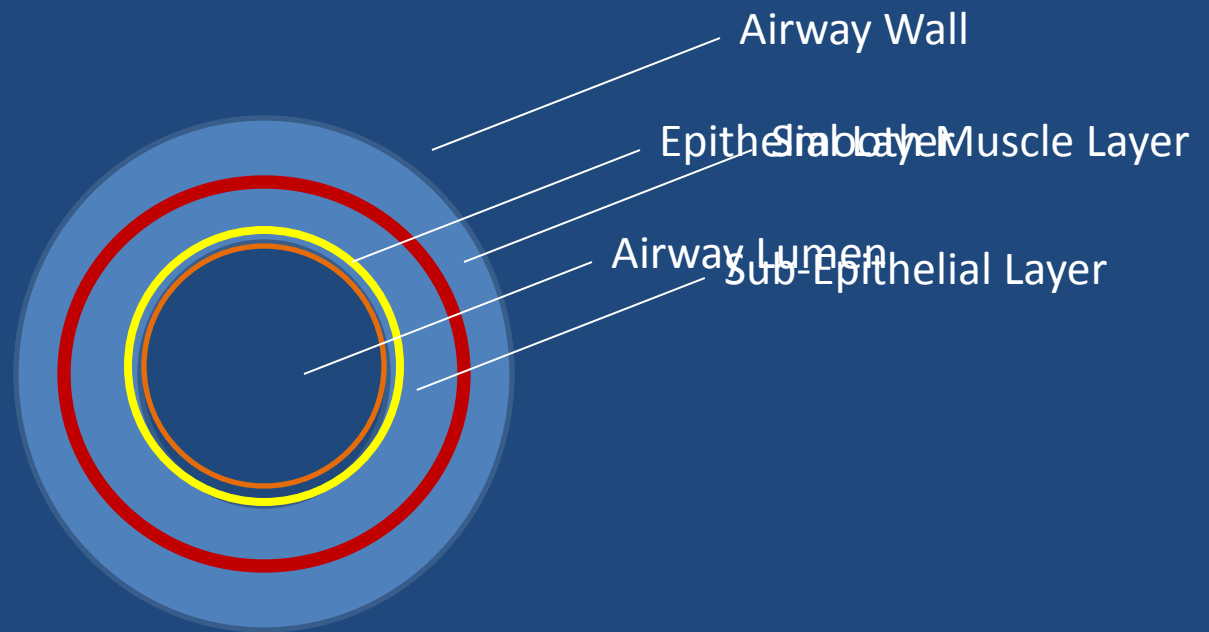
# Disclosures

- No conflicts related to this presentation
- Studied Airway Smooth Muscle as a Fellow
- Currently study asthma medications in clinical trials

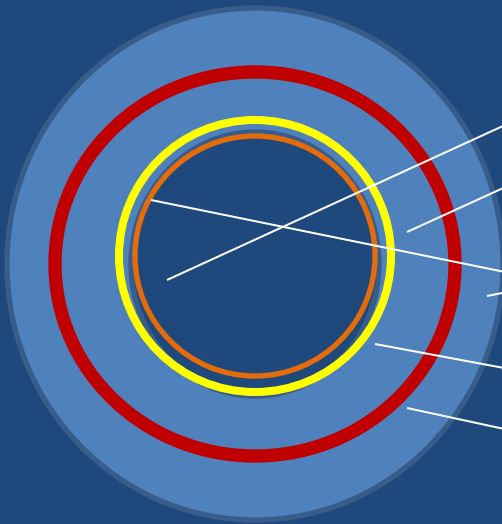
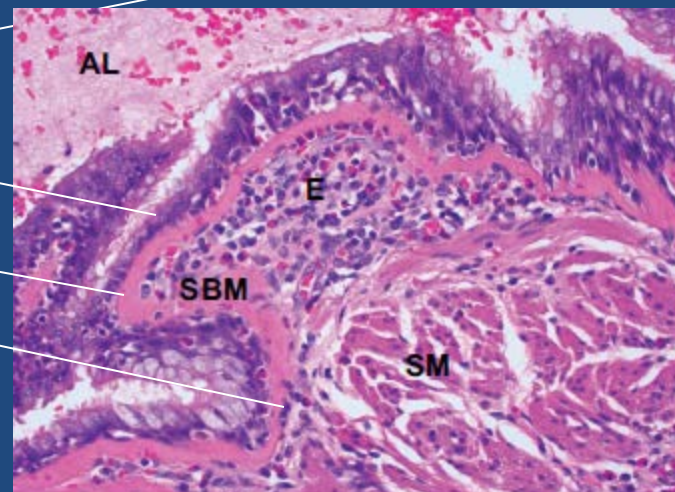
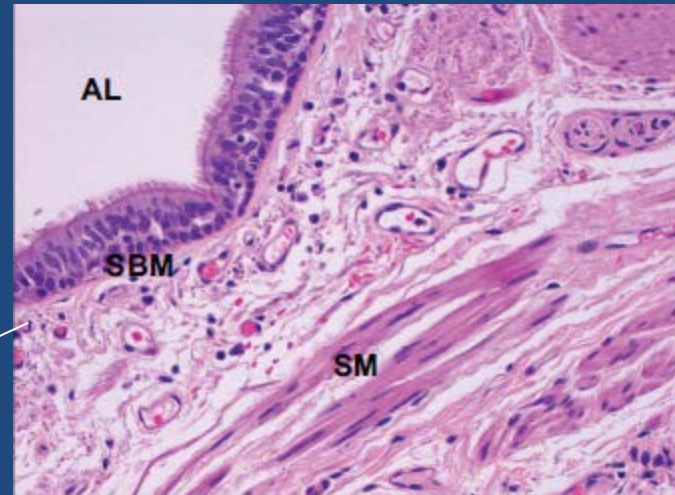
# Airway Remodeling

- Pathology
- Structural Functional Correlates
- Natural History
- Effects of Treatment (or lack thereof)
- In Vitro Models

# Pathology of Asthma



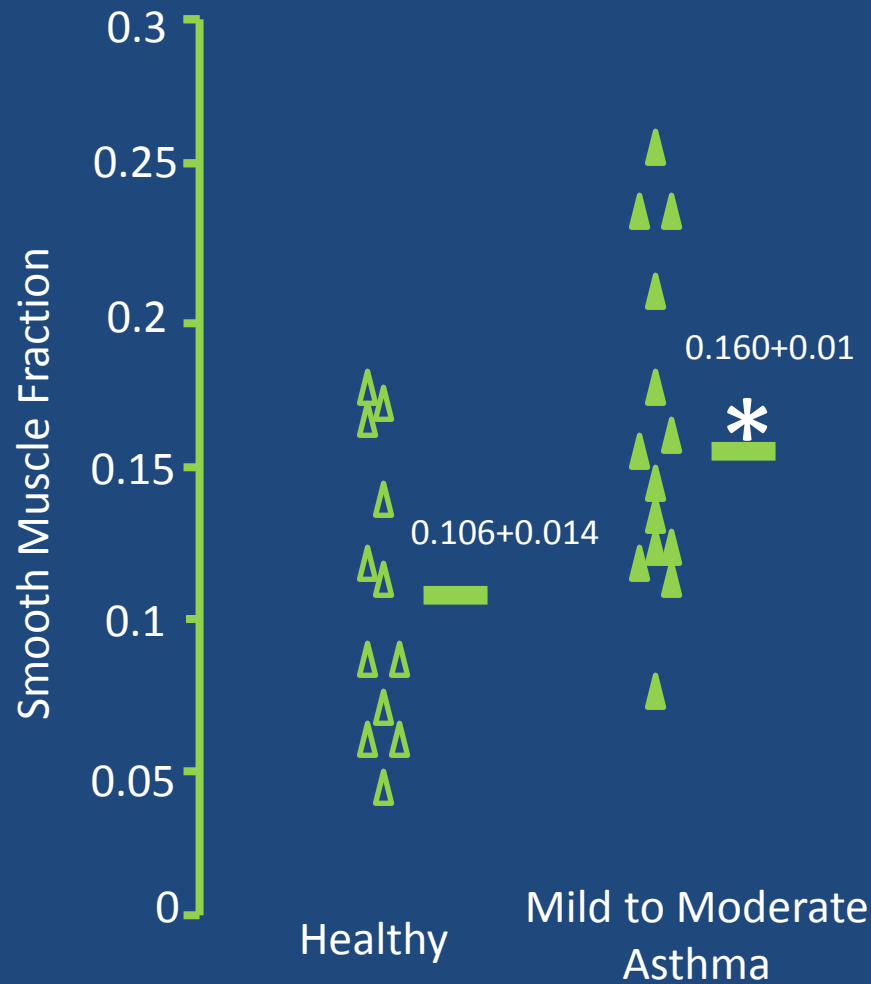
# Airway Remodeling



# Structure/Function

- Limited availability of airway samples
- Functional data often missing
- Endobronchial Biopsies
  - Accurate assessment of ASM difficult
  - More accurate at assessing sub-epithelial layer
- High Resolution CT

# Airway Smooth Muscle: Asthma vs. Control

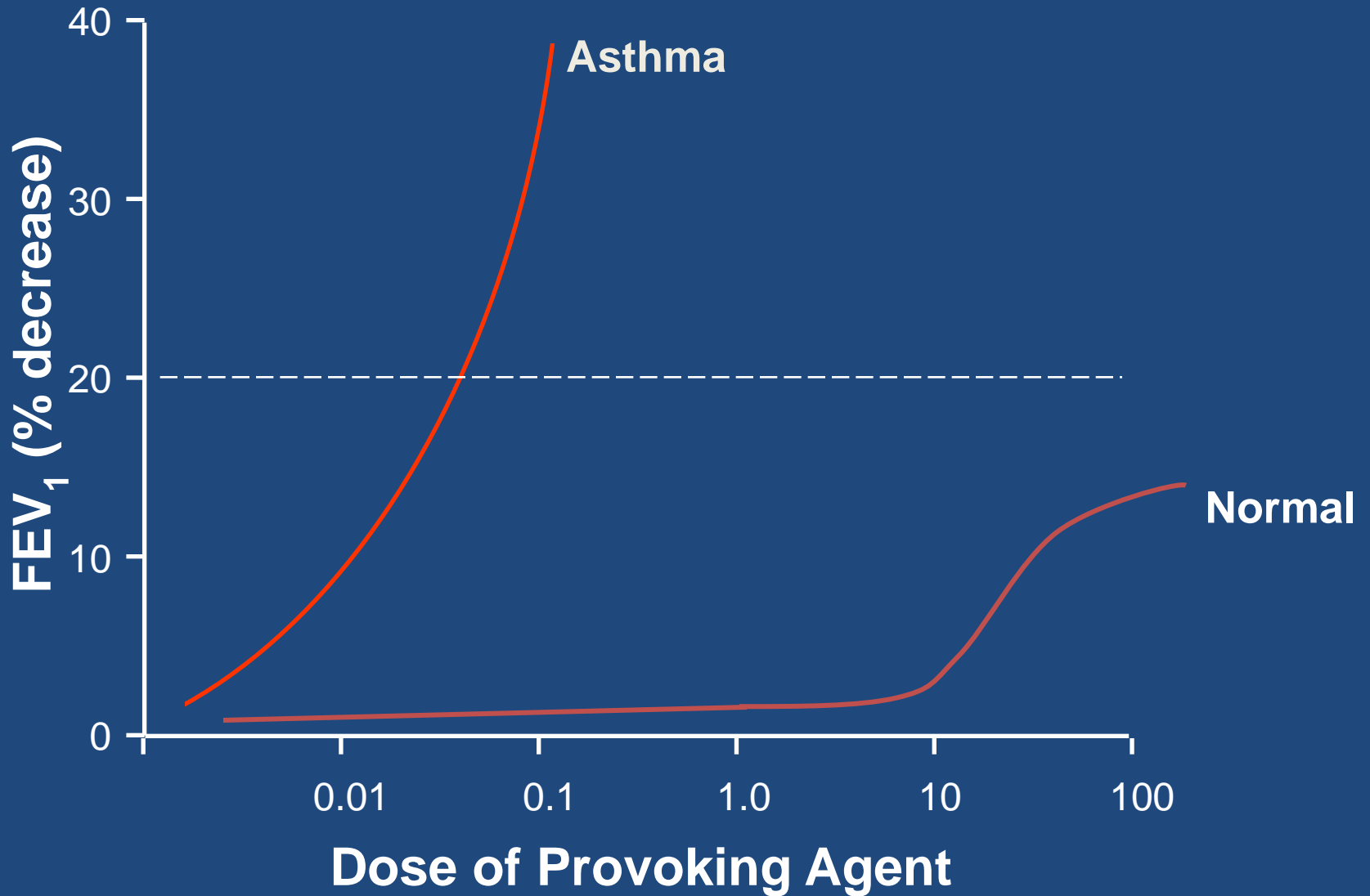


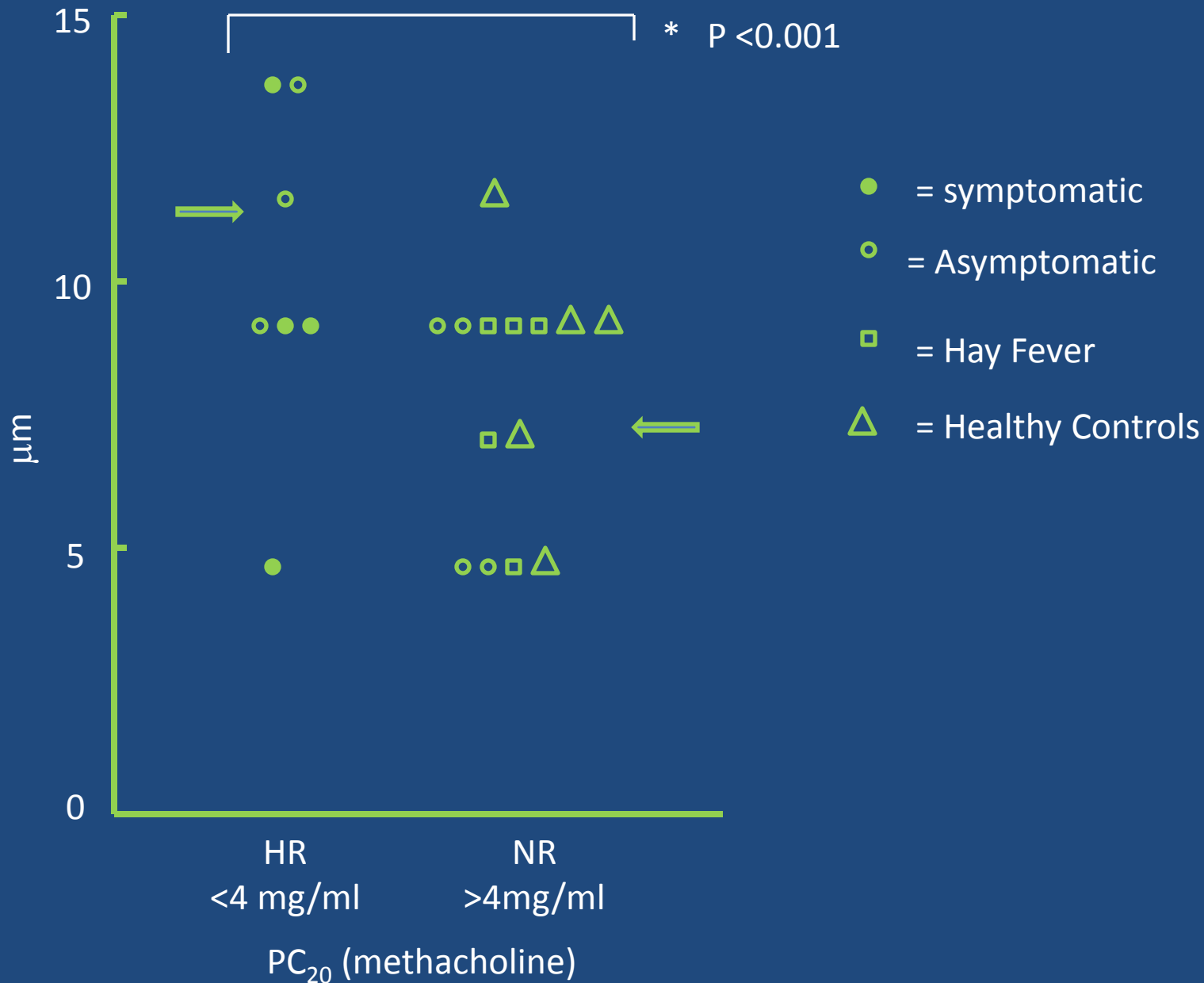
# How to Measure Airway Function in Asthma

- FEV1
- FEV1/FVC
- FEV1/TLC
- Methacholine Challenge

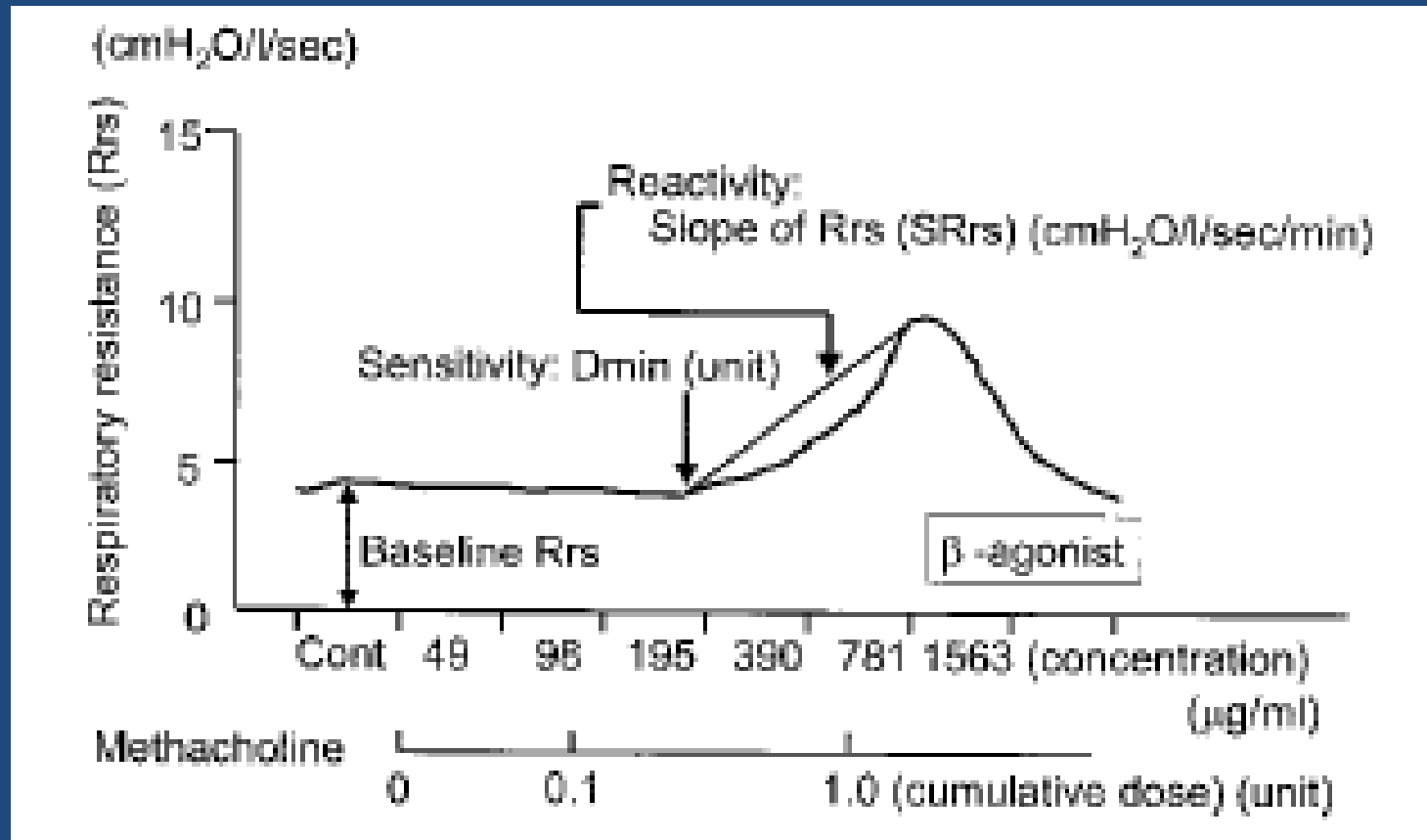


# Methacholine Challenge

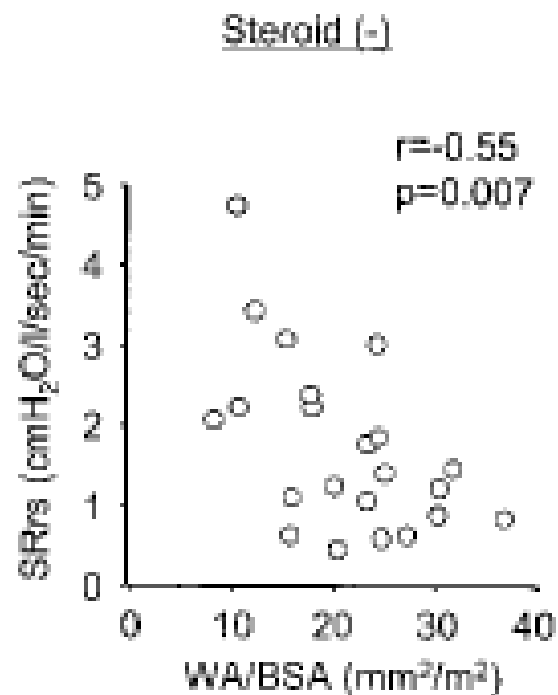
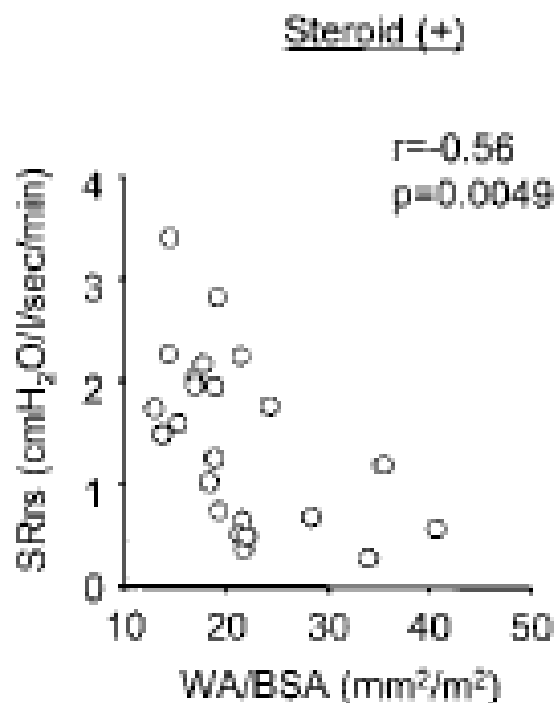




# Continuous Methacholine Challenge

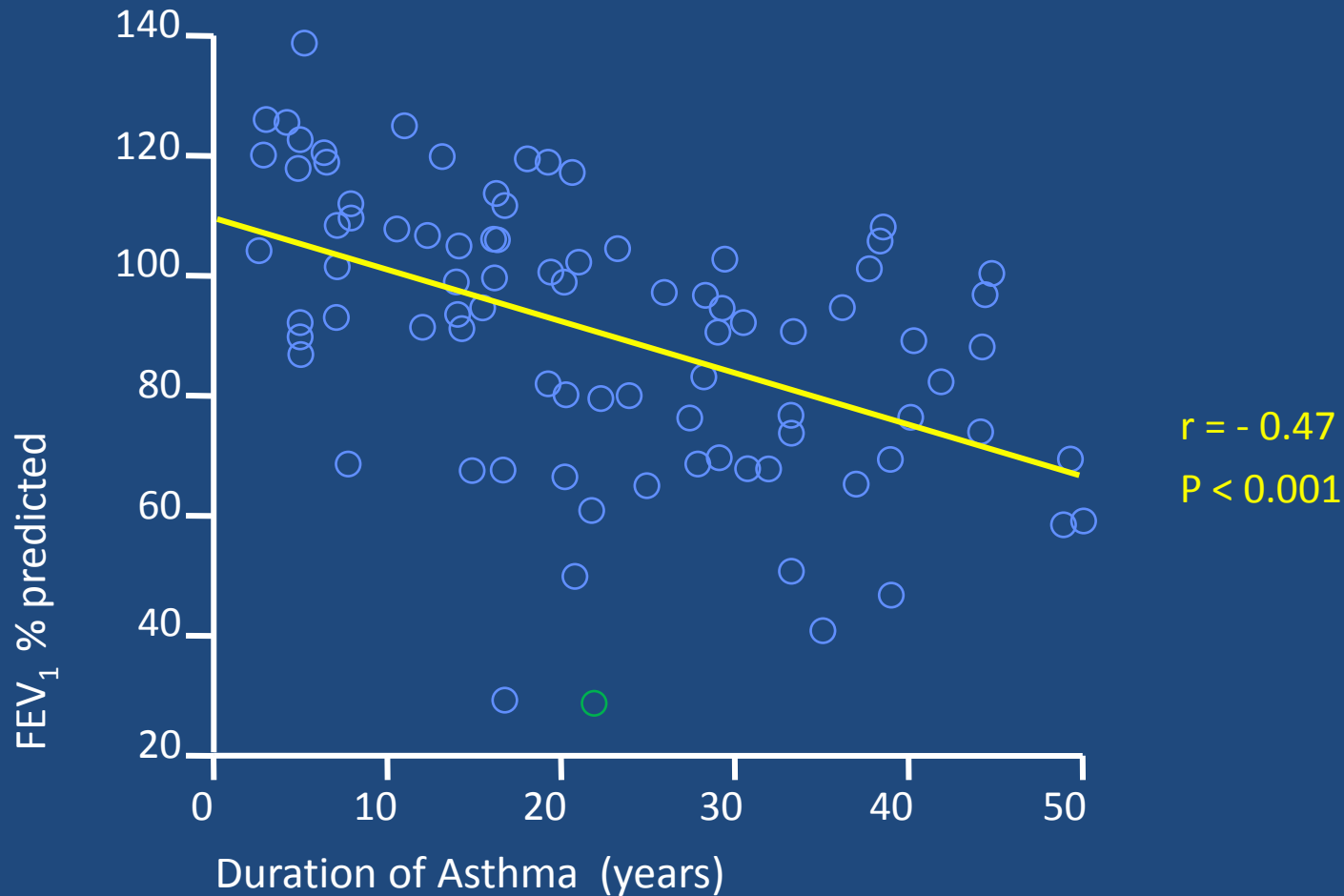


# Wall Thickness by CT vs. Reactivity



# Natural History of Asthma

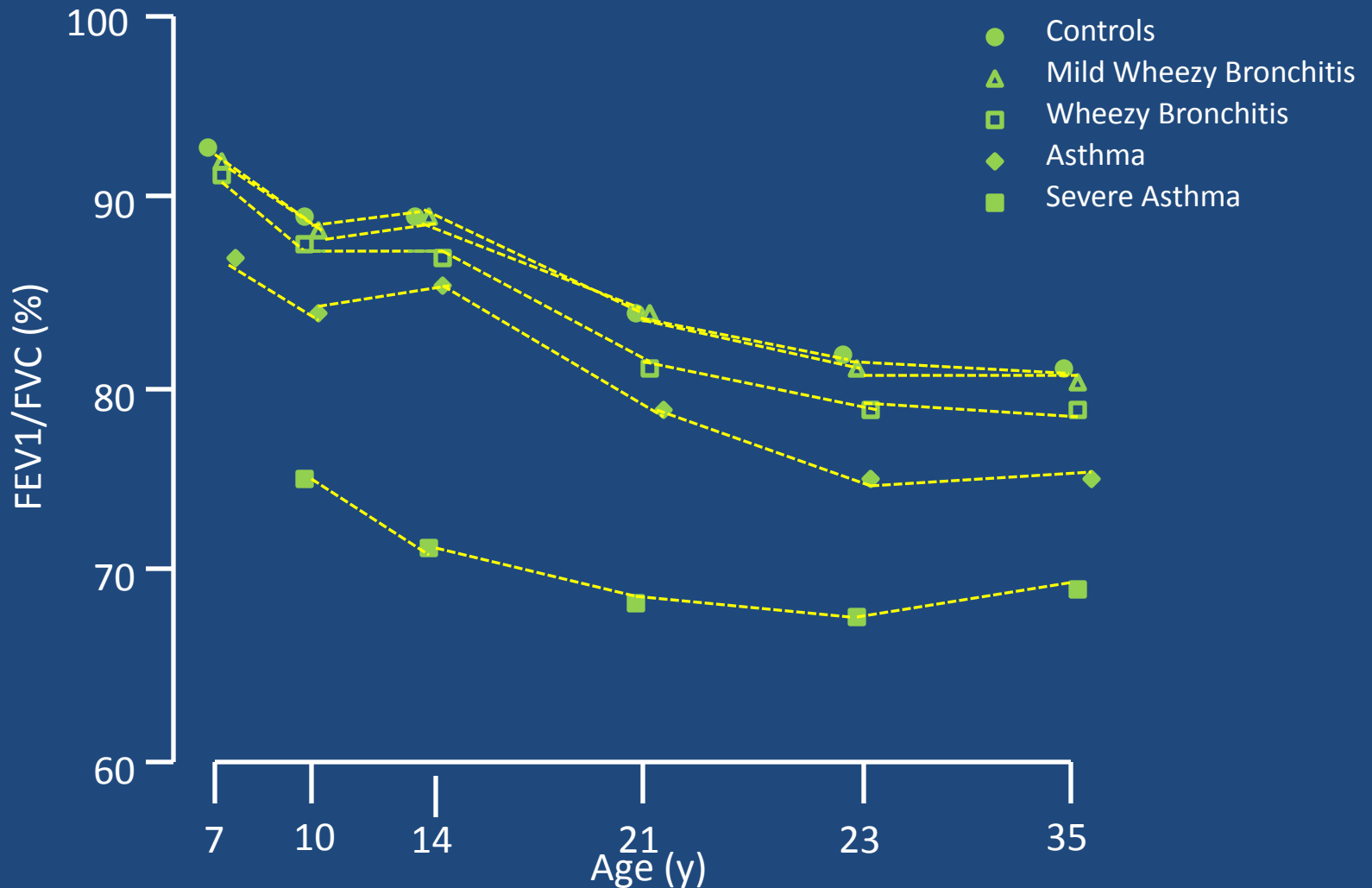
89 well-controlled asthmatics in Australia



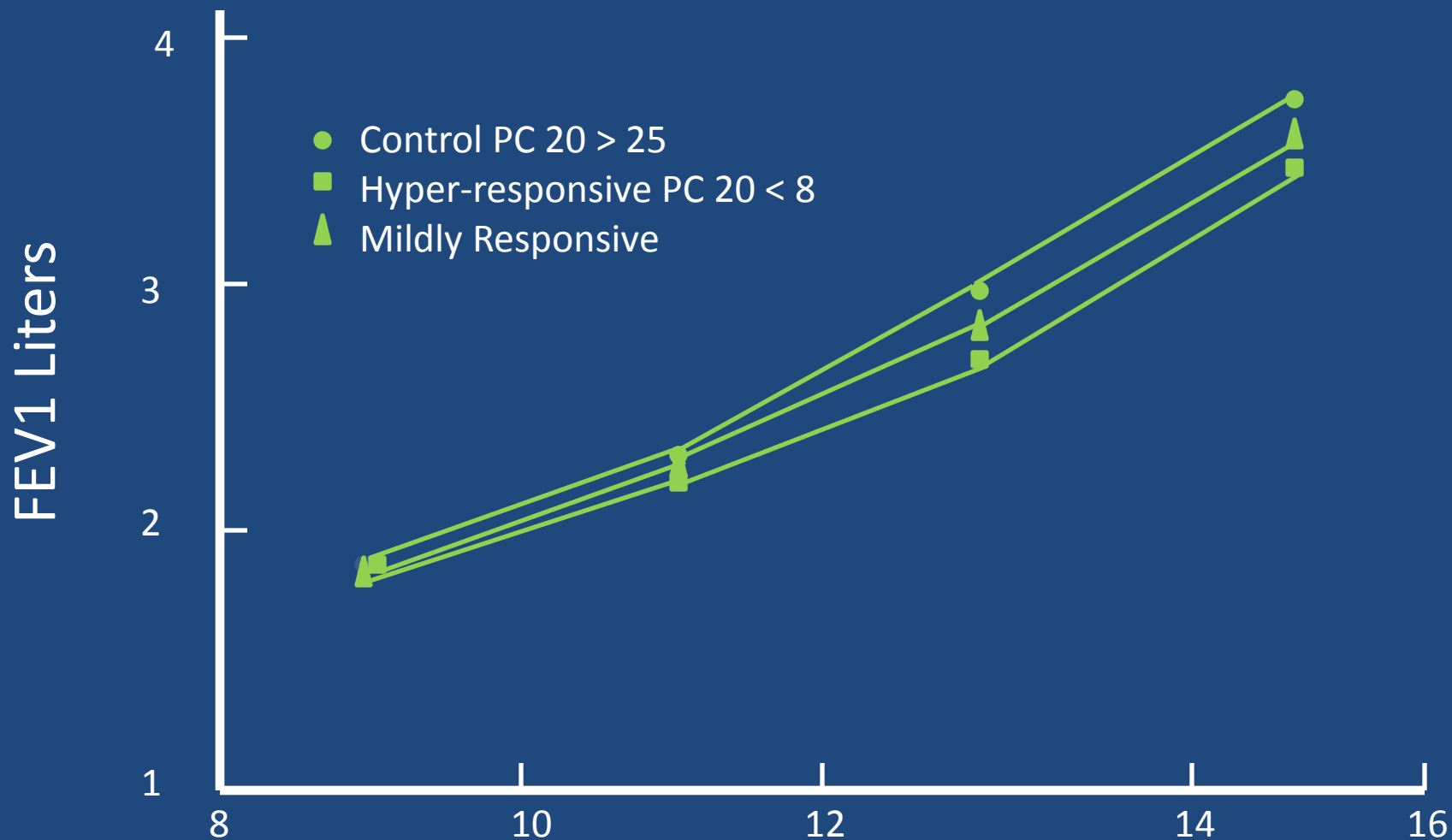
# Melbourne Cohort

- 7 year old School Children
- Asthma or Wheezy Bronchitis
- Mild Wheezy Bronchitis
- Normal
- Follow up at age 10, 14, 21, 28, 35
- Severer asthma cohort added at age 10

# Melbourne Cohort

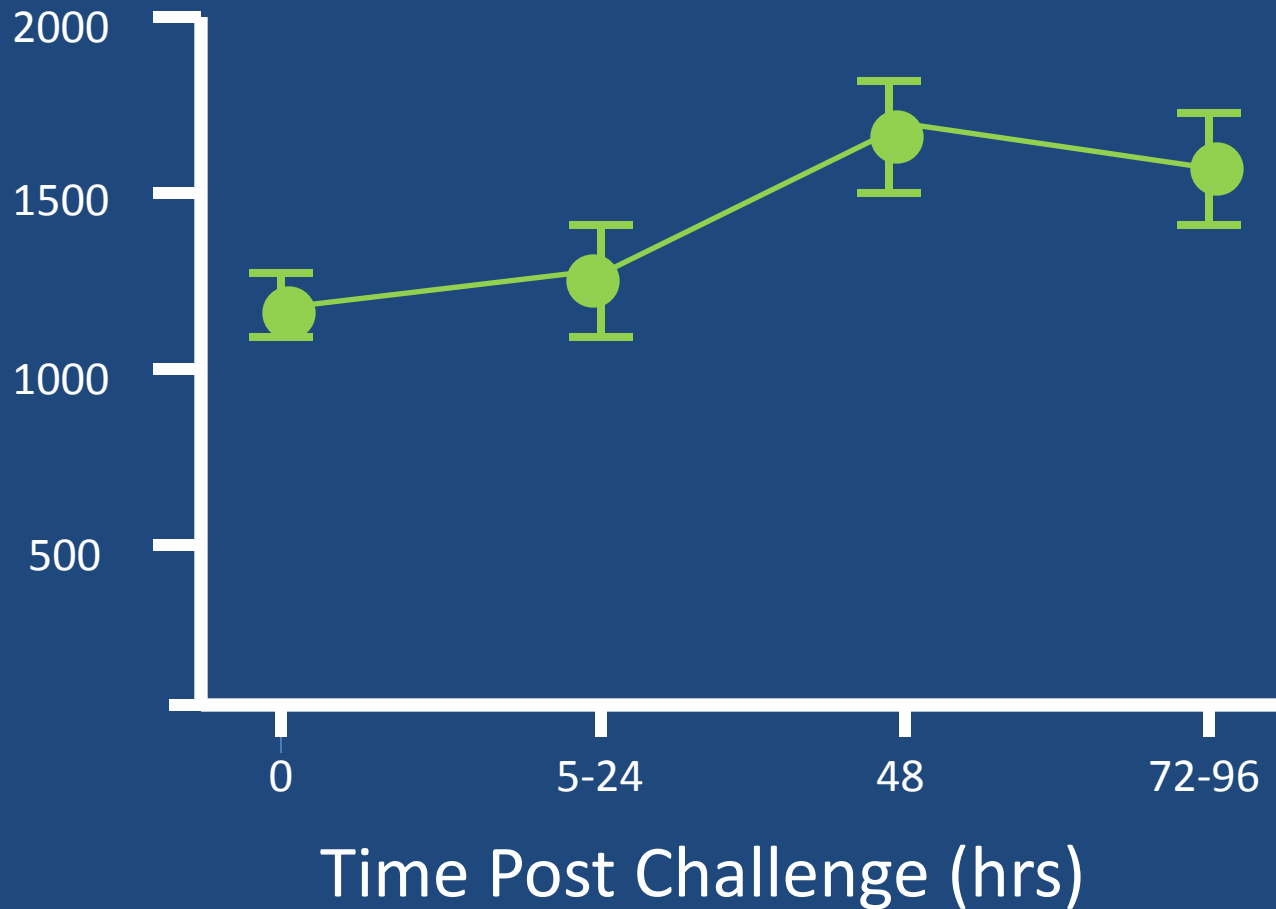


# Reduced Lung Growth in Asthma (New Zealand Cohort)





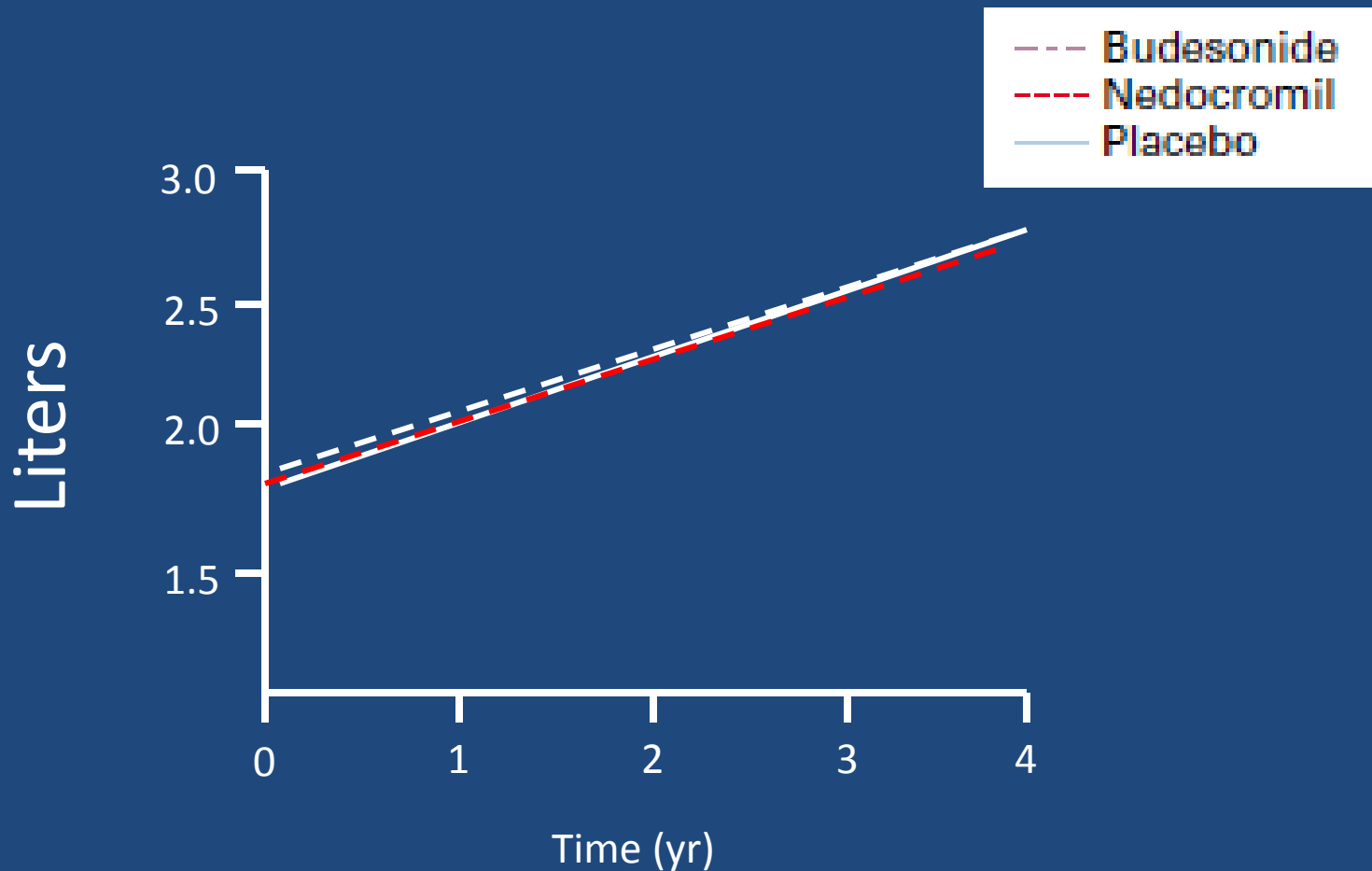
# Allergic Stimulation and Smooth Muscle Growth



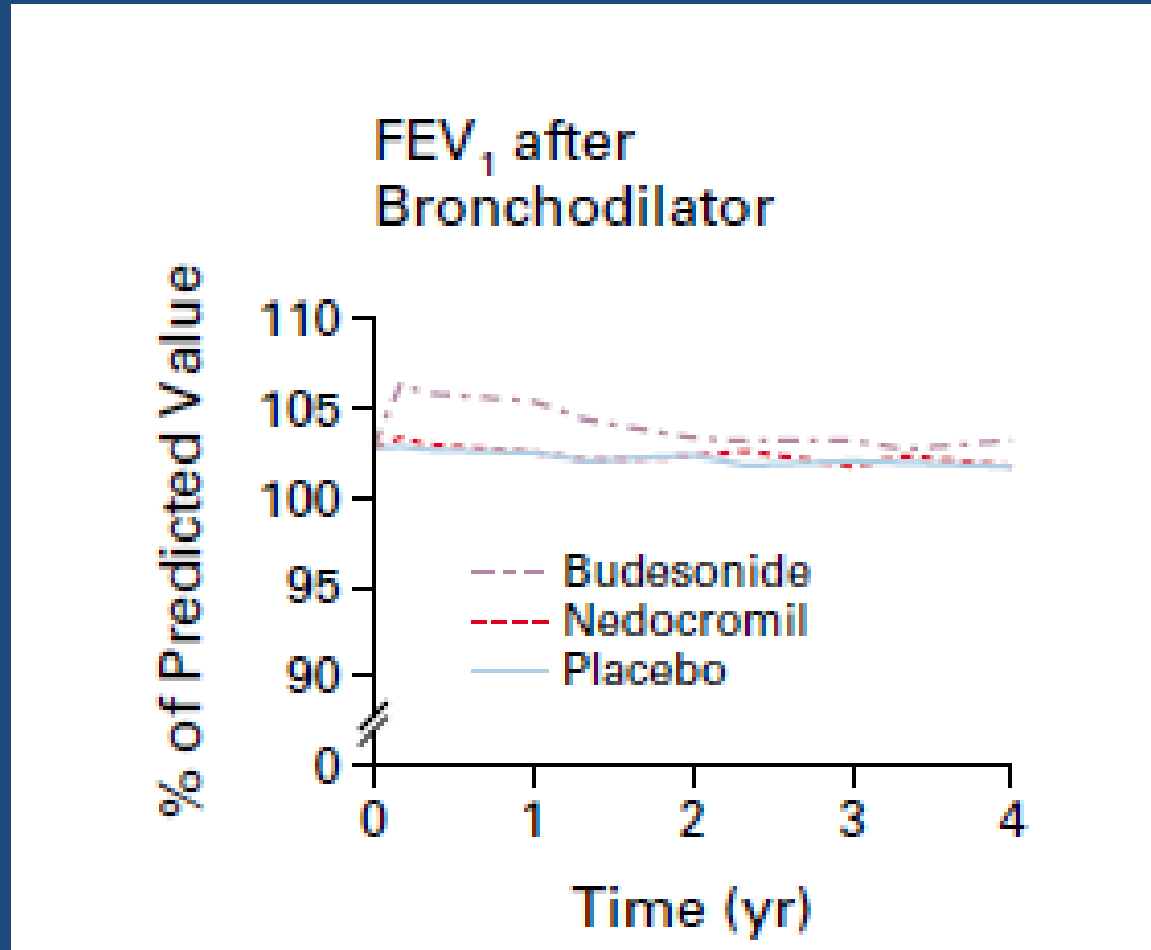
# “Inflammation Leads to Remodeling”

- Inflammation releases growth factors
- Treatment of asthma (ICS) will reduce growth factor release
- Remodeling can be reduced by treatment
- Inflammation should be aggressively treated
- Even in the absence of symptoms or obstruction.

# Childhood Asthma Management Program (CAMP)



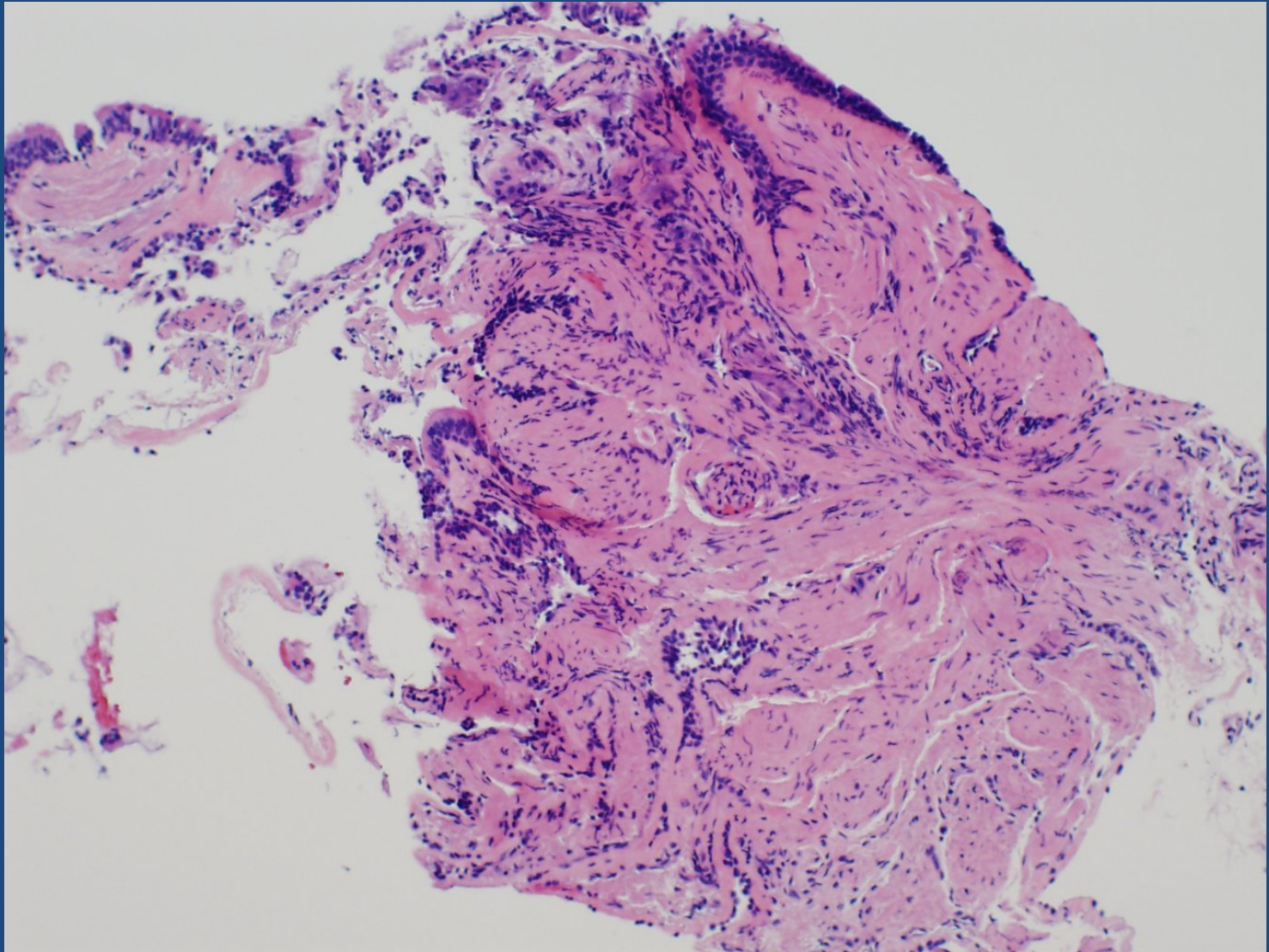
# CAMP



# Why Wasn't Lung Growth Improved?

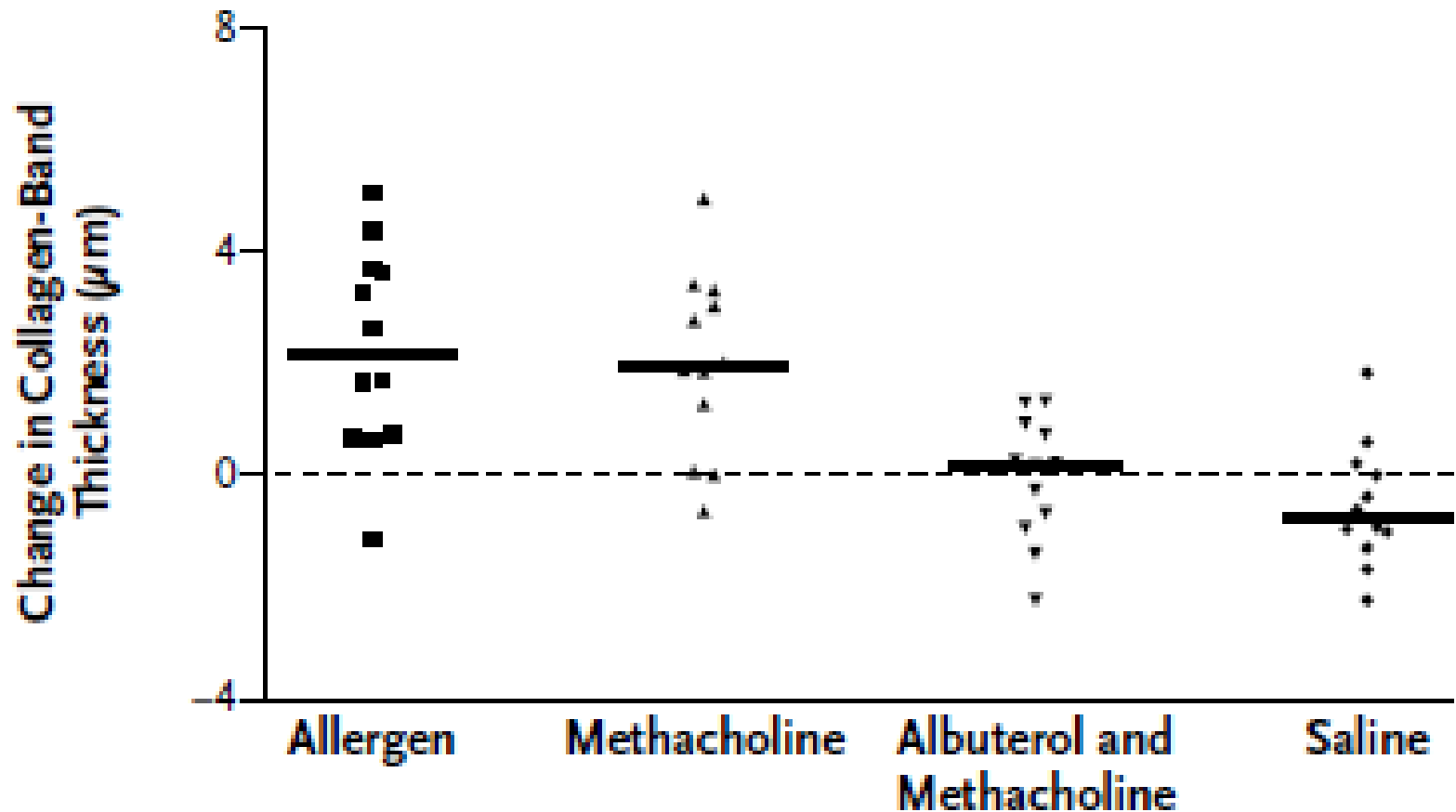
- Inadequate therapy
- Therapy improving inflammation may not affect smooth muscle
- Smooth muscle growth may be independent of inflammation
- Something more fundamental may explain the loss of flow in asthmatics independent of remodeling

# “Pauci-Immune Asthma”

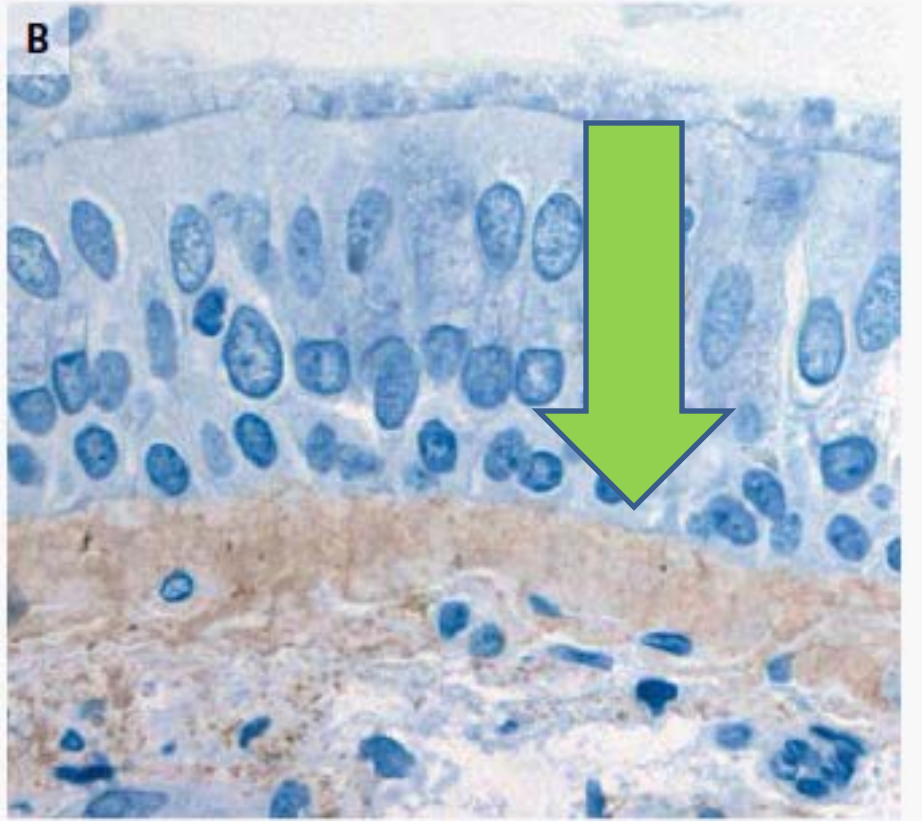
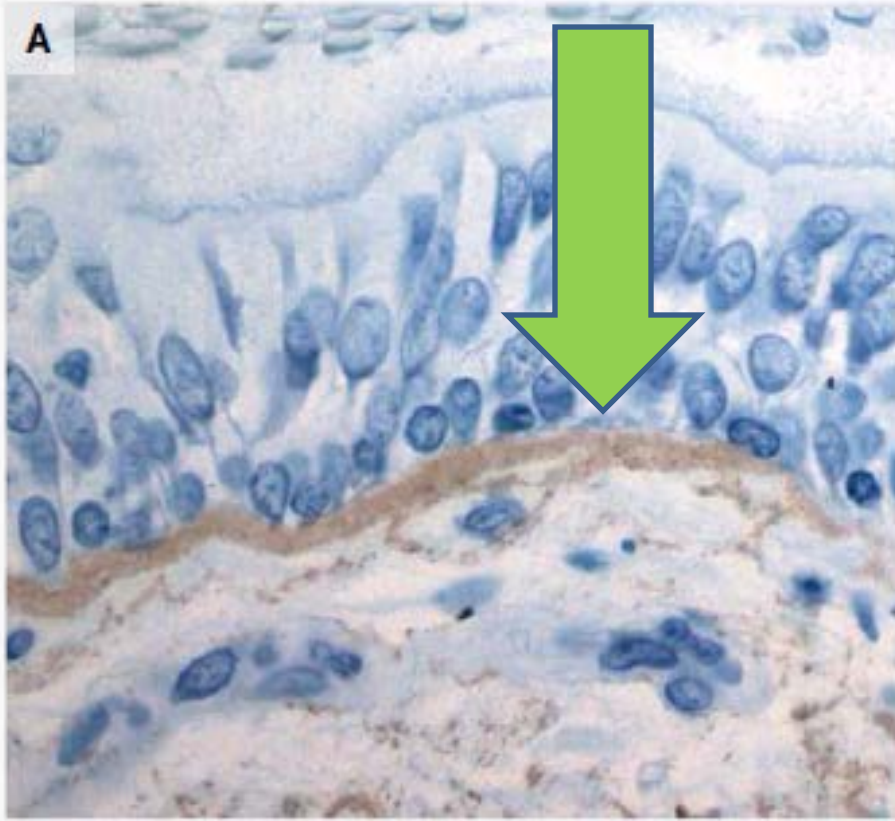


# Non Allergic Stimulus Leads to Subepithelial Thickening

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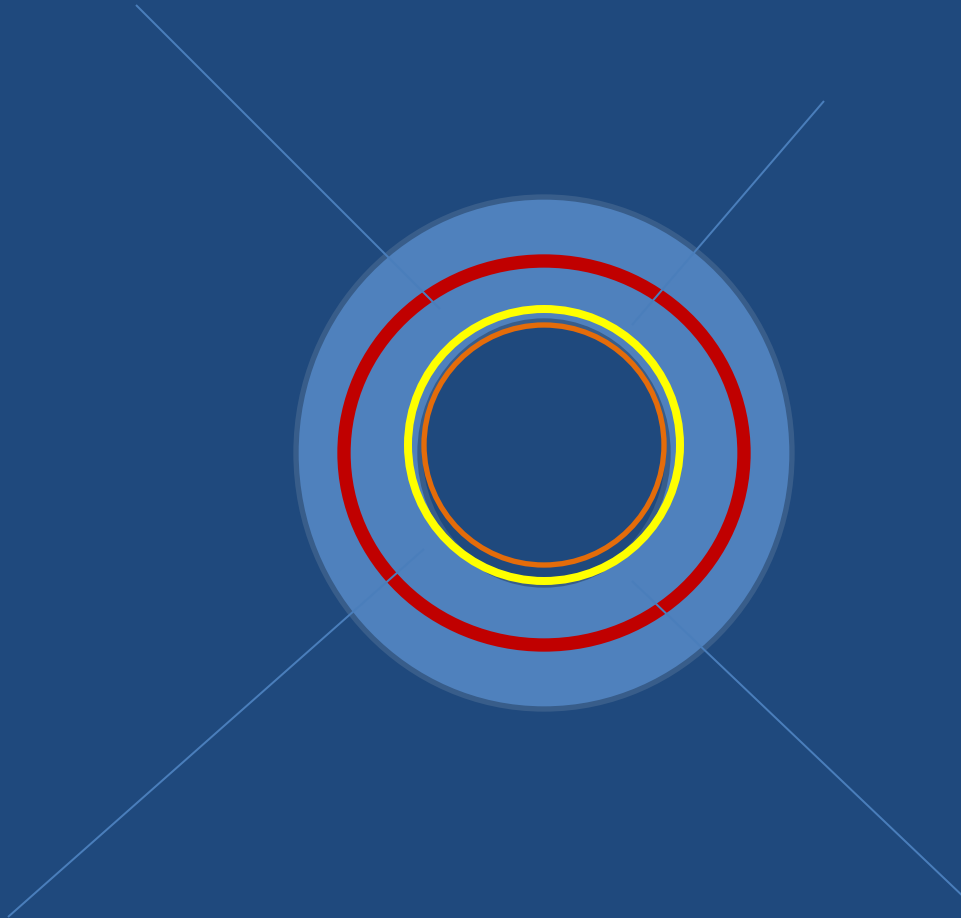




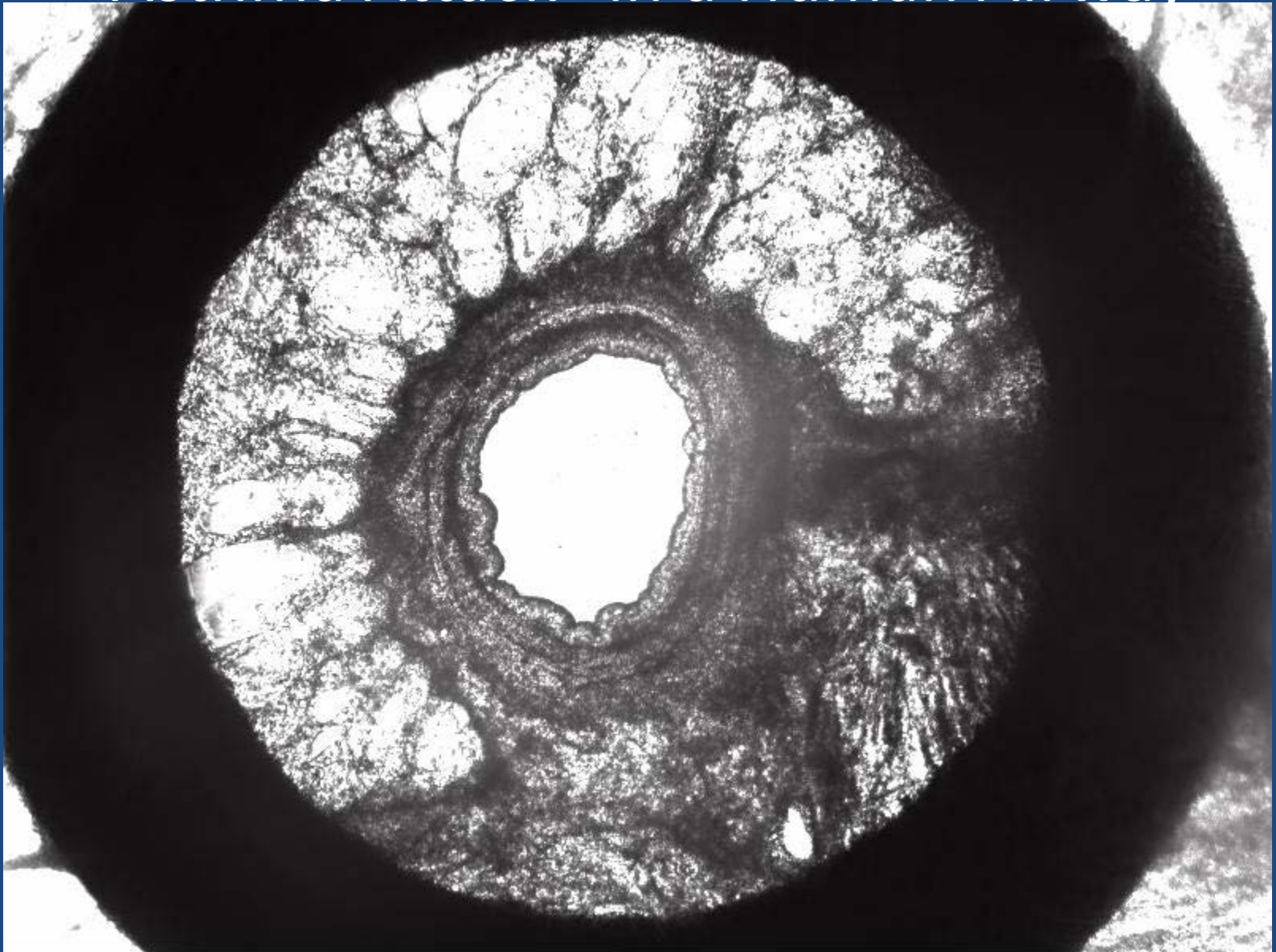


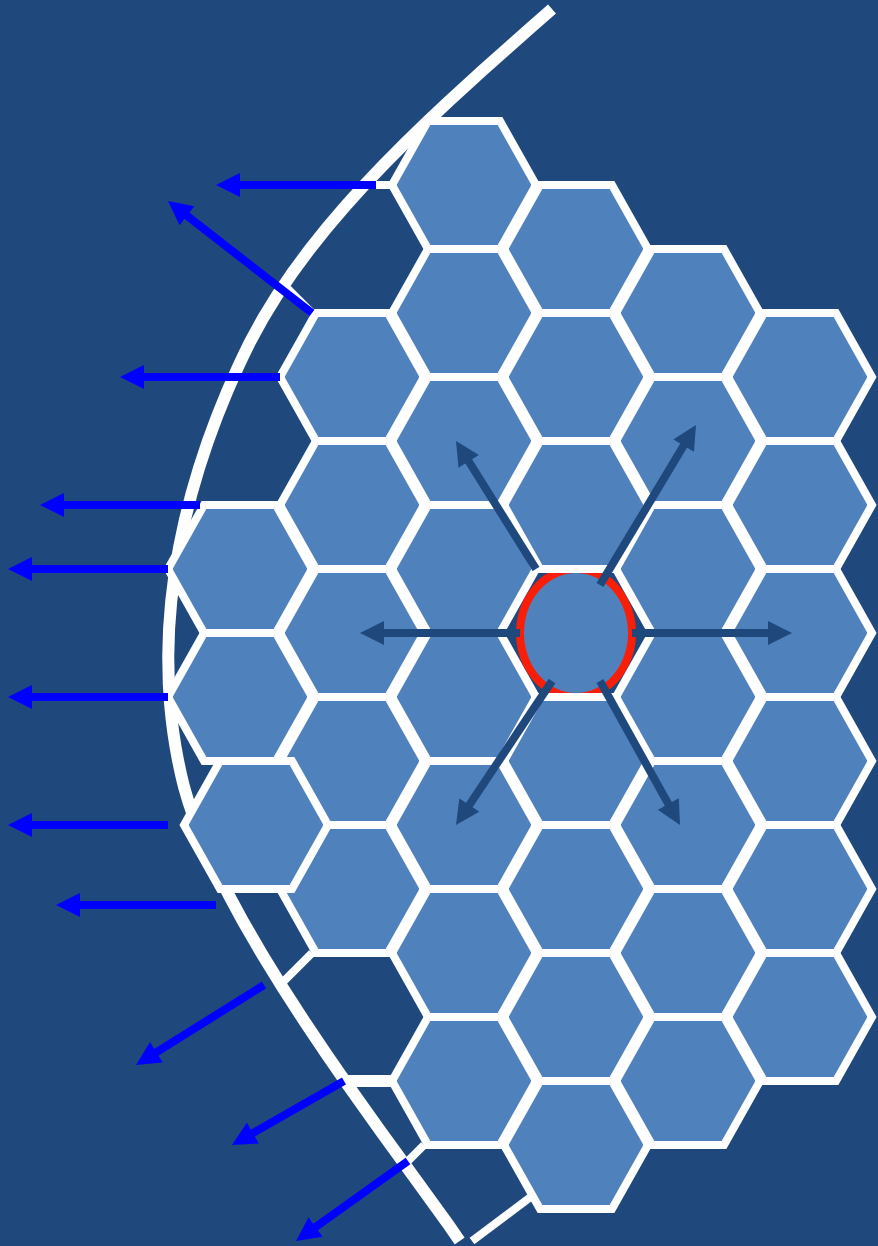


# Airways are Subject to Cyclic Stretch



# “Asthma Attack” in a Human Airway





# Treatment Strategies for Asthma

- EPR 2- Therapy based on severity
  - No clear provision for tapering therapy
- EPR 3- Therapy based on control and risk
  - If control is maintained for 3 months can attempt to reduced therapy
  - Therapy is stepped up if patient has frequent exacerbations or sx uncontrolled

# Conclusions

- Airway modeling occurs in asthma
- Remodeling Changes can be correlated with alterations in lung function
- Unclear whether treatment of inflammation can alter the course of airway remodeling
- Treat based on symptoms and risk of exacerbation rather than to alter remodeling
- Newer therapies may be needed to reduce ASM amount and contractility