Asthma Pathophysiology

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Definition of Asthma

- Chronic inflammatory disorder of the airways
  - Mast cells, eosinophils, T lymphocytes, macrophages, neutrophils, epithelial cells
- Causes variable and recurrent episodes of wheezing, breathlessness, chest tightness, cough – especially at night or early morning
- Associated with widespread, but variable airflow obstruction that is often reversible

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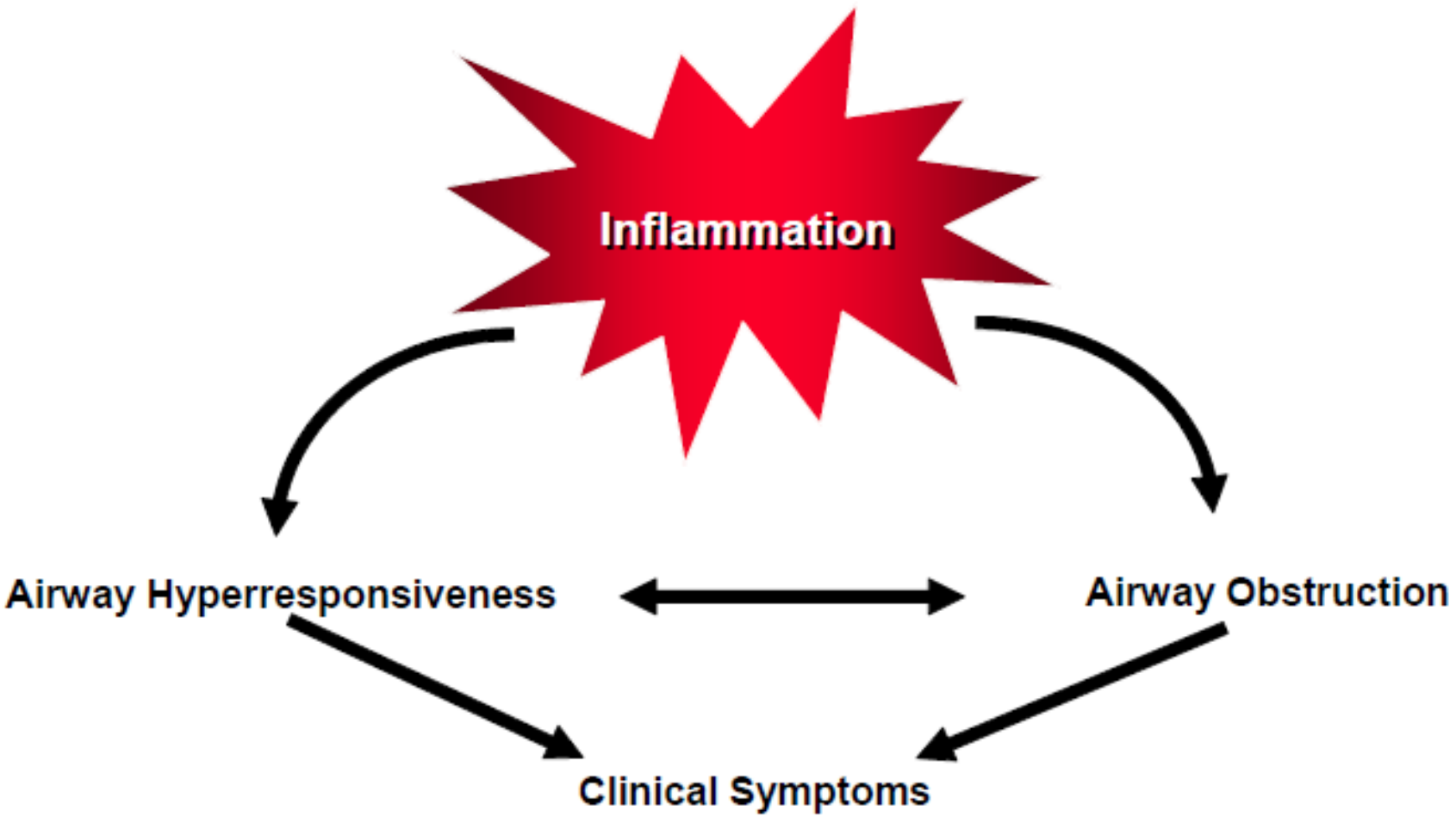
FIGURE 2–1. THE INTERPLAY AND INTERACTION BETWEEN AIRWAY INFLAMMATION AND THE CLINICAL SYMPTOMS AND PATHOPHYSIOLOGY OF ASTHMA



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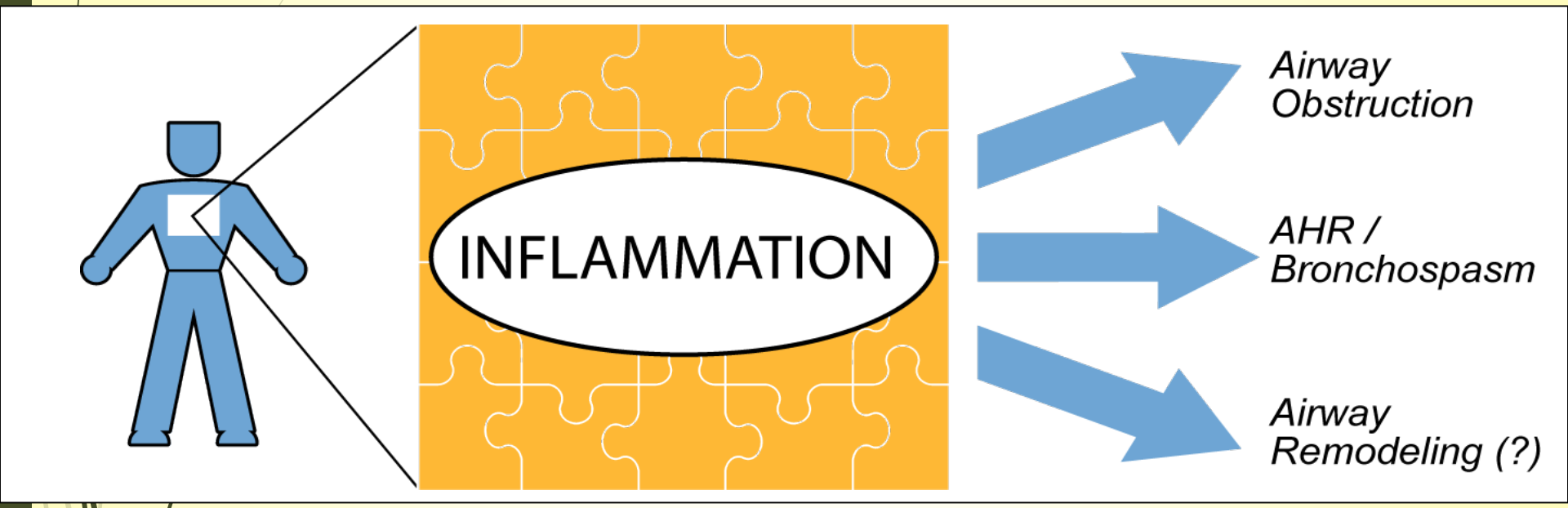
Asthma Pathophysiology

Individual **Inflammation** **Impact**



Genetic predisposition
Intrinsic vulnerability
Gene-environment interact:
Atopy / allergy
Infection

Inflammation underlies disease processes

Phenotype varies by individual and over time

Clinical symptoms also vary by individual and over time

AHR = airway hyperresponsiveness

Airflow Limitation

- Induced by airway inflammation
  - Bronchoconstriction- Bronchial smooth muscle contraction that quickly narrows the airways in response to exposure to a variety of stimuli
  - Airway hyperresponsiveness- an exaggerated bronchoconstrictor response to stimuli
  - Airway edema- as the disease becomes more persistent and inflammation become more progressive, edema, mucus hyper secretion, and formation of inspissated mucus plugs further limit airflow.

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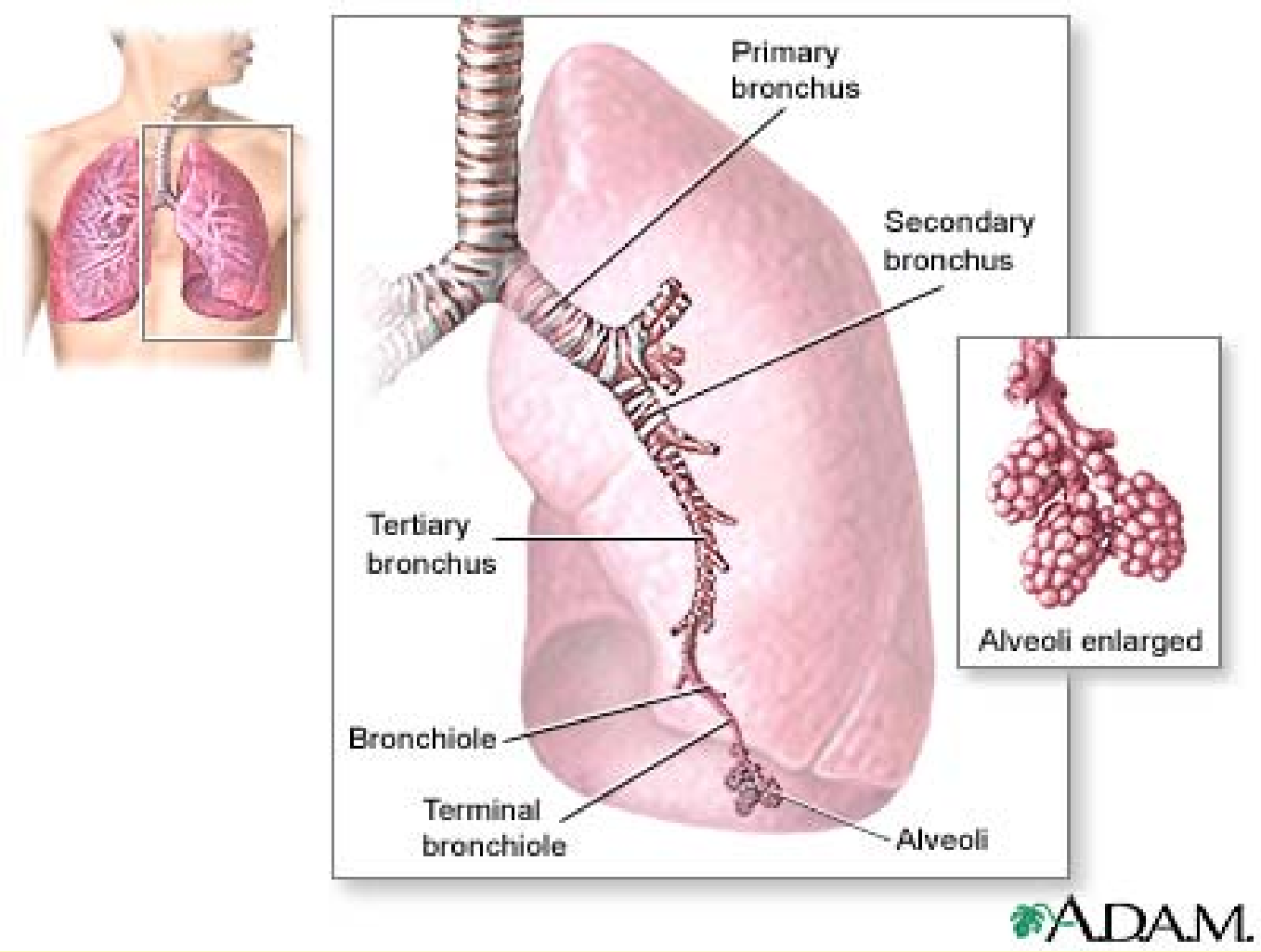
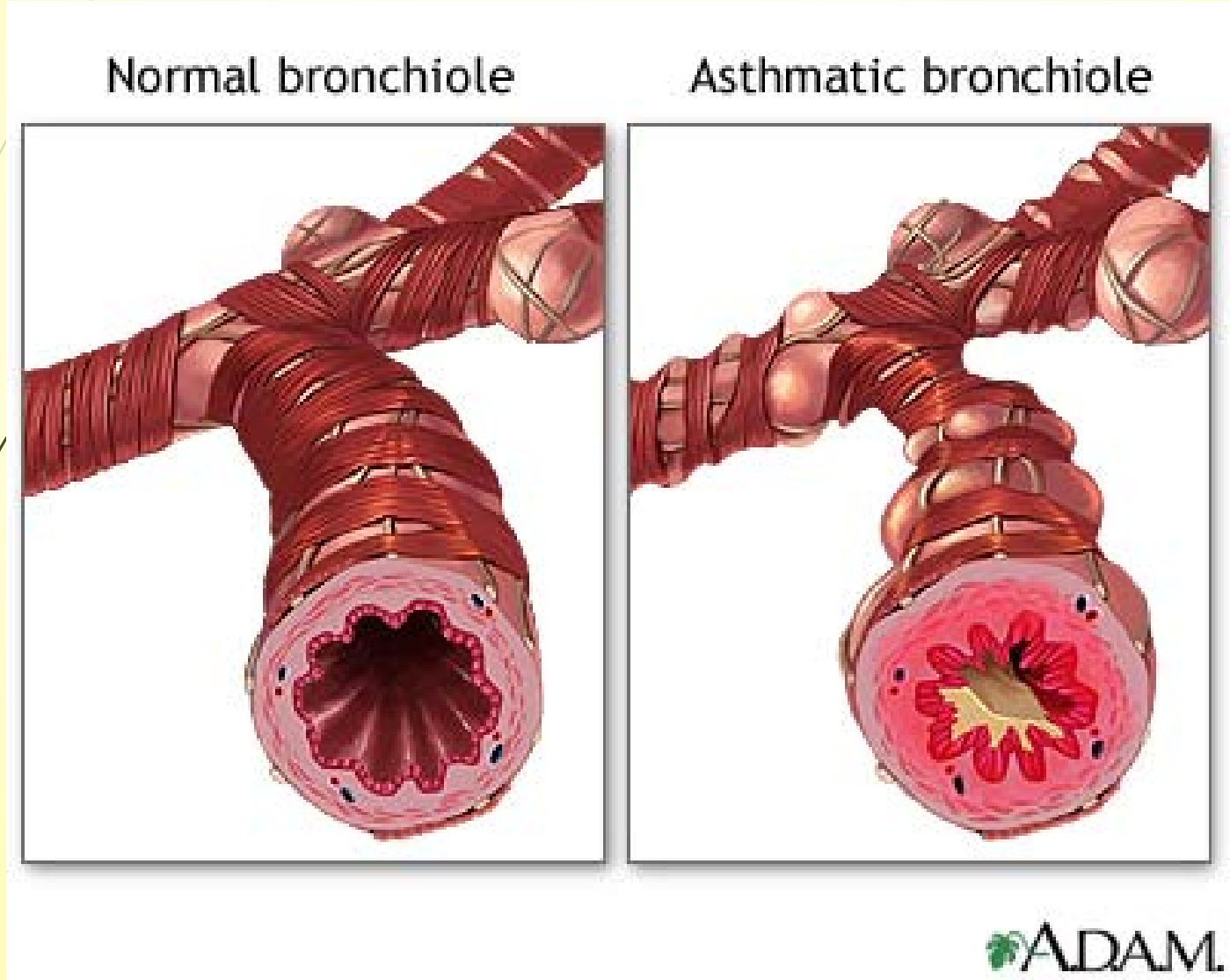
Pathophysiology



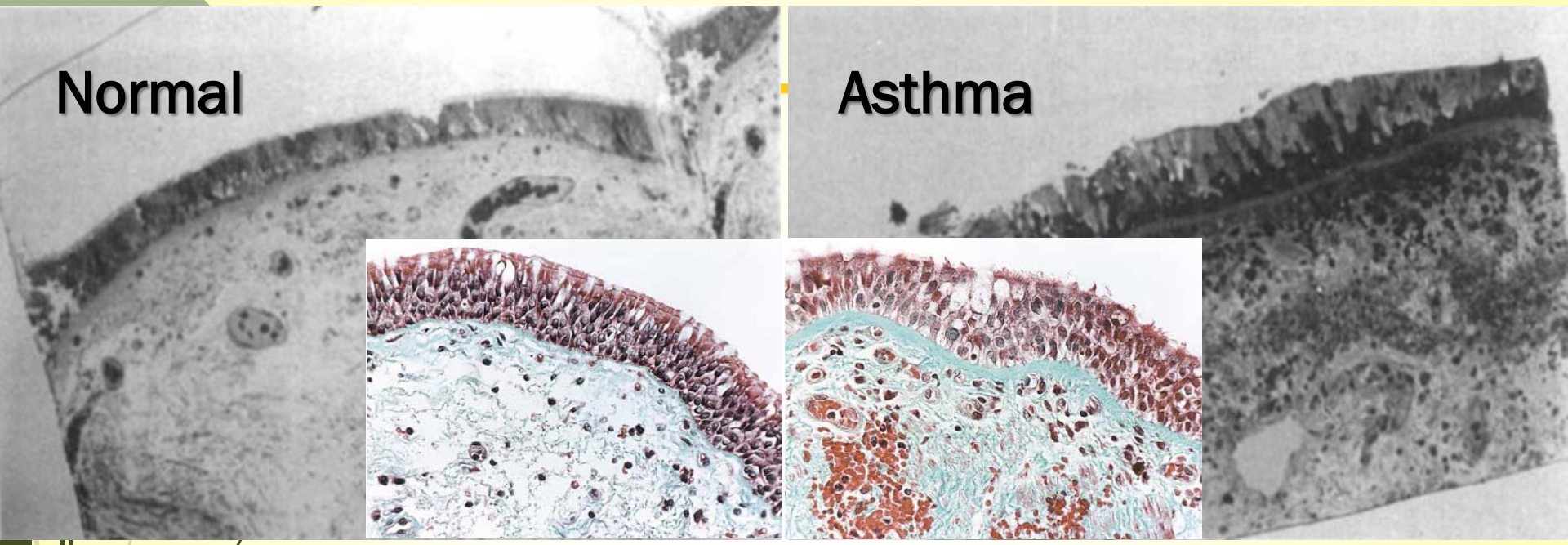
Pathology



Remodeling

- Reversibility of airflow limitation may be incomplete in some patients.
- Persistent changes in airway structure
  - Sub-basement fibrosis
  - Mucus hypersecretion
  - Injury to epithelial cells
  - Smooth muscle hypertrophy
  - Angiogenesis

Histopathology of asthma



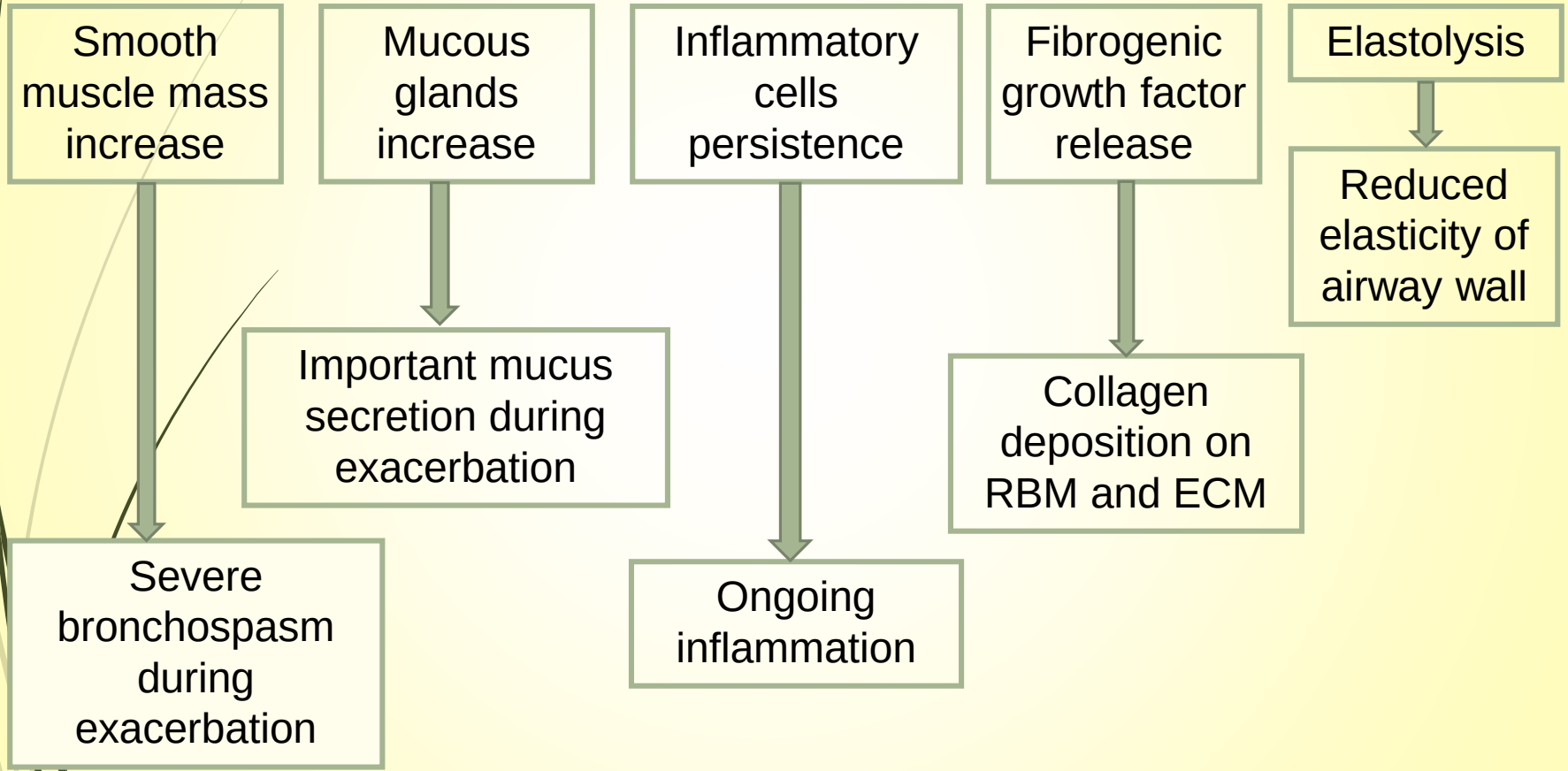
Same in both pictures (x *300)*

- Tight structure with a predominance of ciliated epithelial cells.
- Only few goblet cells in the epithelium.
- The lamina propia, is practically cell-free.
- Inflammatory cells are not seen.

- Less ciliated cells
- Goblet cells hyperplasia
- Epithelium and lamina propia are highly infiltrated (mainly eosinophils and lymphocytes)
- Edema
- Basement membrane thickening
- Collagen deposition in the sub mucosa

Laitinen et.al. Allergy Proc 15,6:323, 1994

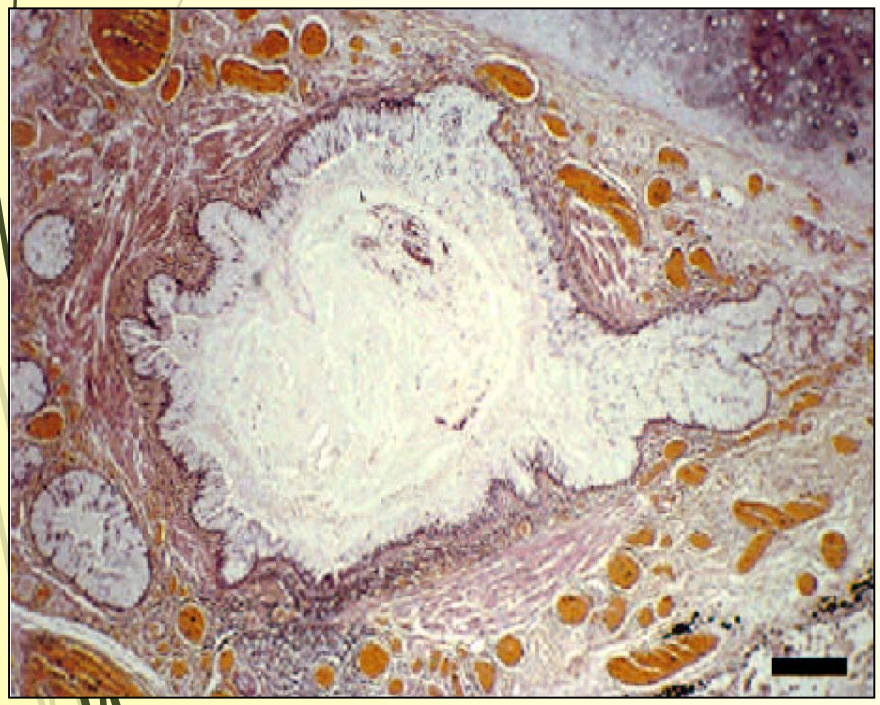
Consequences of Remodeling in Asthma

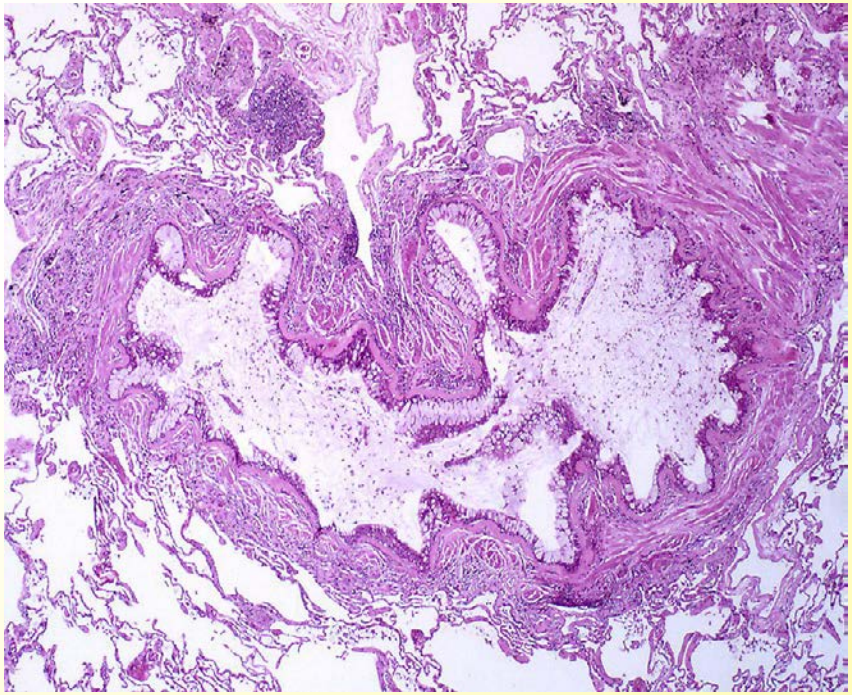


Bousquet J, et al. *Am J Respir Crit Care Med*. 2000;161(5):1720-1745.

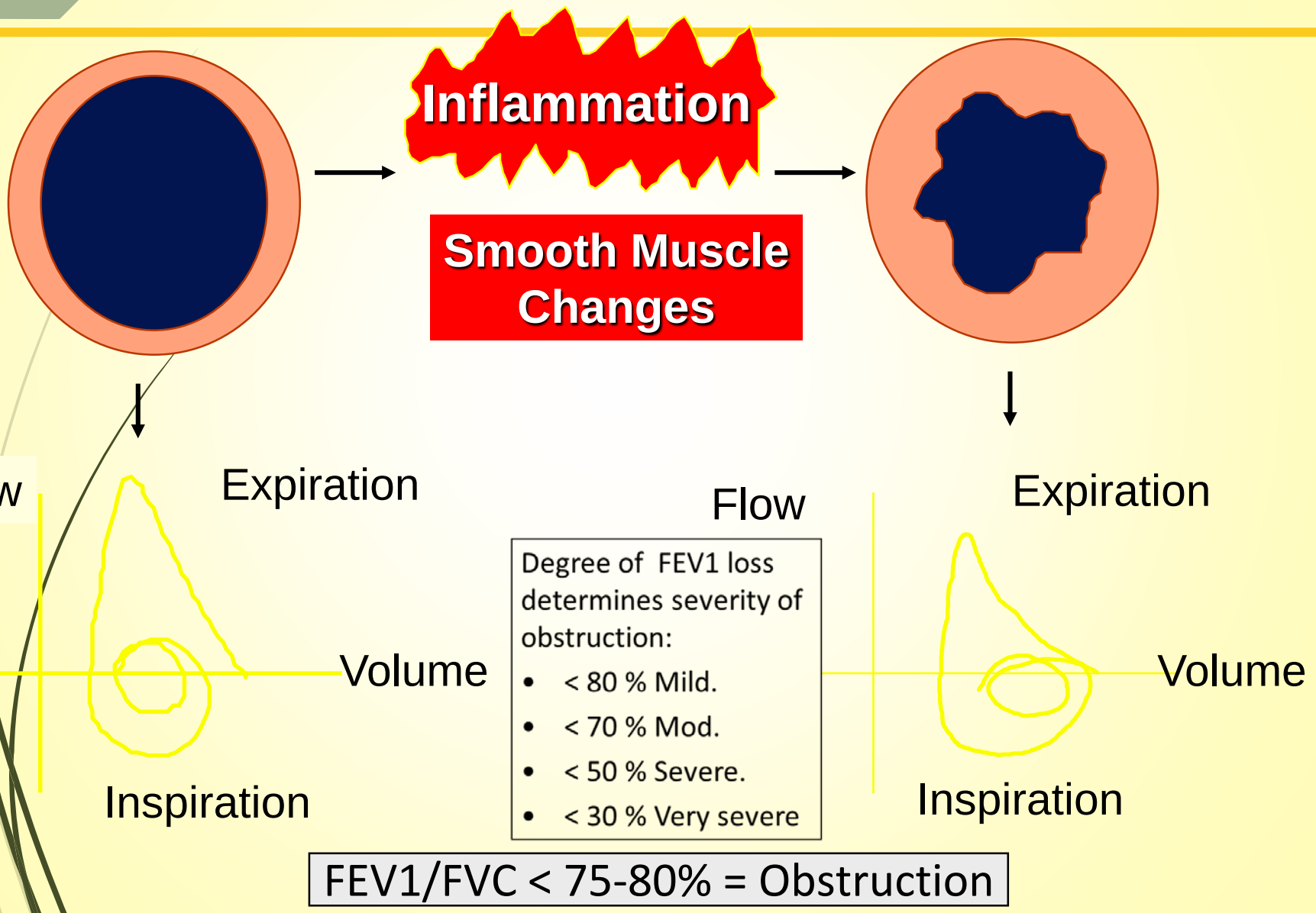
Histopathology of Status Asthmaticus

In fatal exacerbations the pathology is dominated by extensive plugging of the conducting airways with mucus and extracellular debris





Changes in the Asthmatic Airway

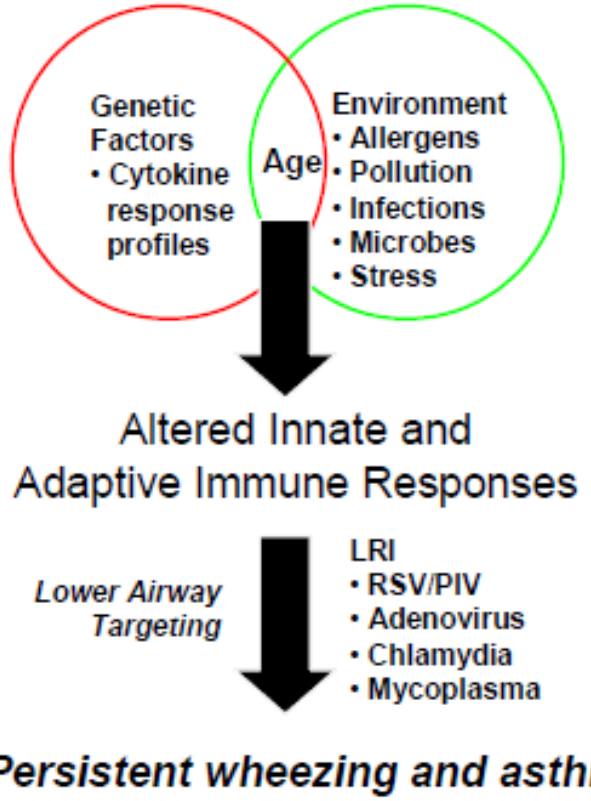


Causes of Asthma

- Interplay between host factors (primarily genetics), and environmental exposures that occur at a crucial time in the development of the immune system.
- A definitive cause is unknown.

Causes of Asthma

FIGURE 2–4. HOST FACTORS AND ENVIRONMENTAL EXPOSURES



Key: LRI, lower respiratory illnesses; RSV, respiratory syncytial virus; PIV, parainfluenza virus

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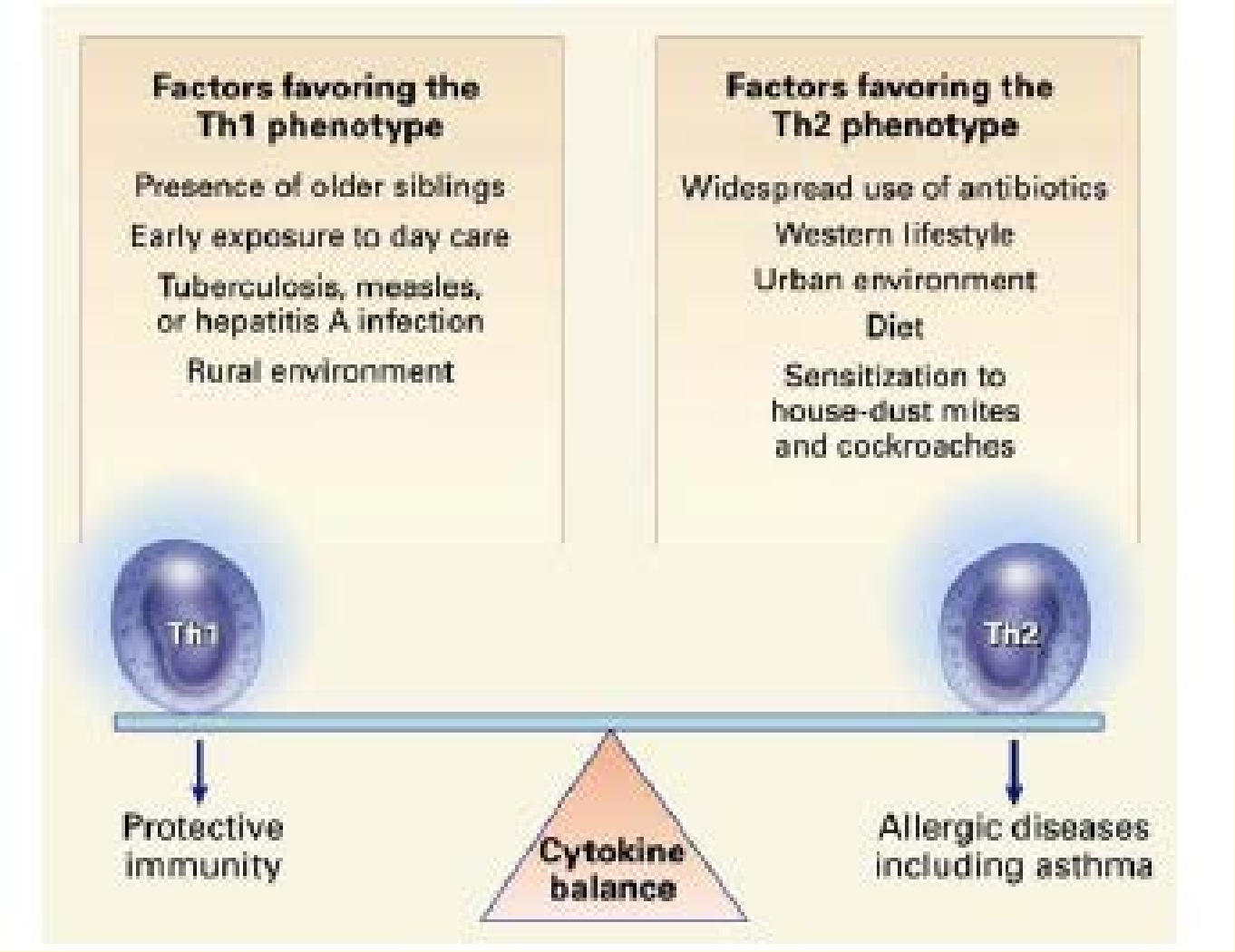
Clinical Heterogeneity of Asthma

- Allergic versus nonallergic asthma
- Late- versus early- onset asthma
- Exercise-induced asthma
- Nocturnal asthma
- Asthma with prominent symptom of cough

Pathogenesis of Asthma



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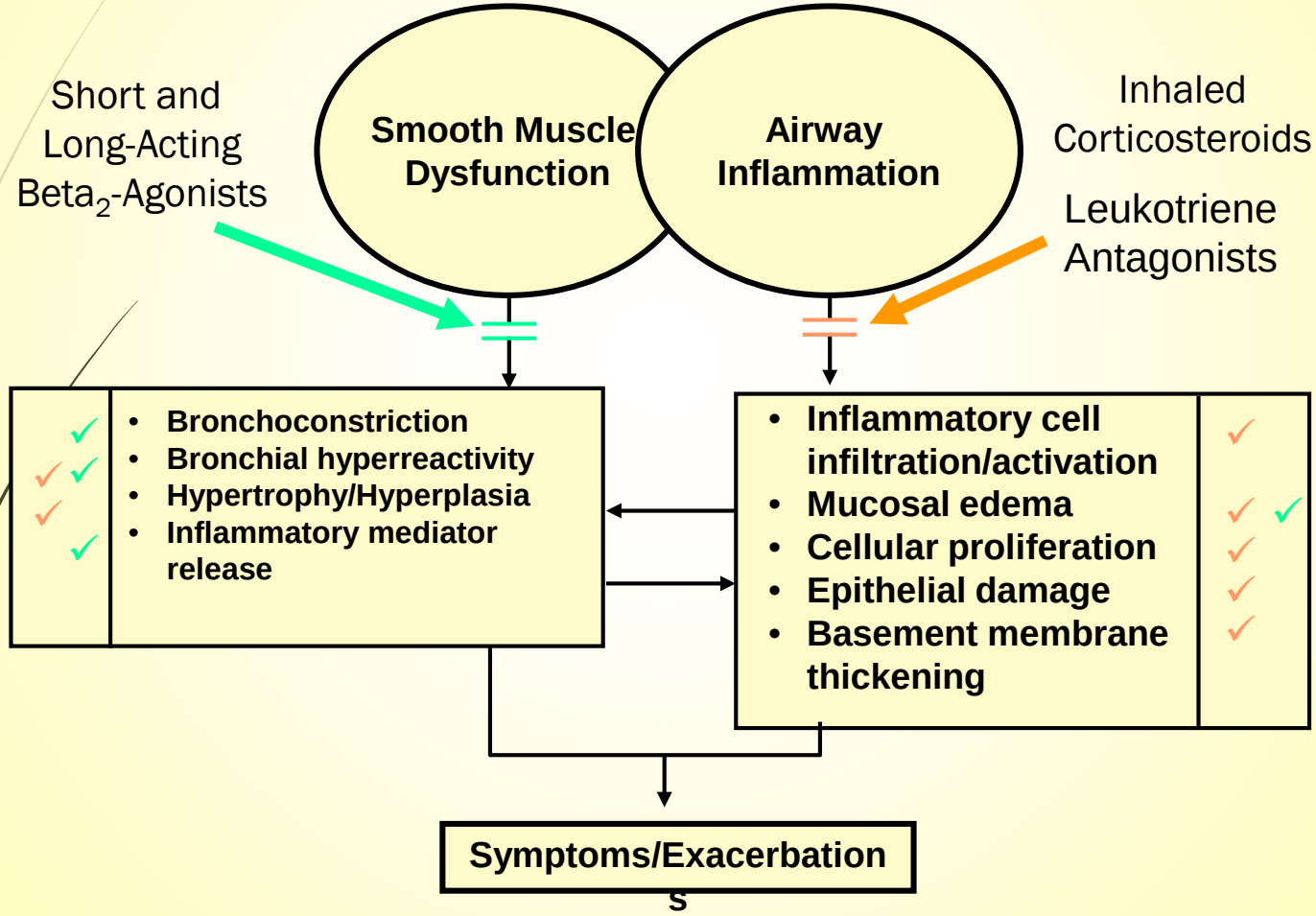
Asthma Pathophysiology –Therapeutic Implications

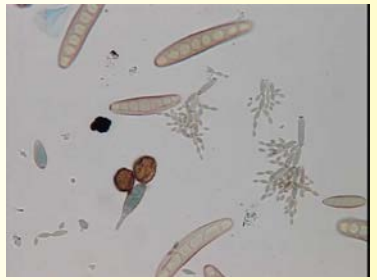


Adapted from Bousquet et al. *Am J Respir Crit Care Med*. 2000;161:1720-1745.

Environmental Factors

- Allergens
  - House dust mite
  - Alternaria
  - Cockroach/mouse
  - Pets

- Infections
  - Atopic interaction
  - RSV, parainfluenza – young
  - Rhinovirus



- Others
  - Tobacco smoke
  - Pollution/Occupation
  - Obesity?

Natural History of Asthma - Children

- Majority of persistent asthma symptoms begin before age 3
- Younger onset (< 3yo vs >6 yo) is associated with lower FEV1 at 11-16 yrs (Morgan 2005, CAMP 2000)
- Majority of asthmatics < 3yo will not wheeze at > 6yo

Asthma in Adults

- Evidence for lower overall lung function in adults with asthma (James, 2005)
- Variable information about rate of decline, when other factors (smoking, COPD) excluded (Sherrill 2003, Griffith 2001)

Questions?