

PATHOGENESIS OF ASTHMA IN CHILDREN

Components of Airway Limitations

- Acute Bronchoconstriction
- Airway Edema
- Mucus Plug Formation
- Airway Injury and Repair



Implications of Asthma Inflammation

- Airway Hyper-responsiveness
- Airflow limitation
- Respiratory symptoms:
 - coughing
 - wheezing
 - shortness of breath
 - chest tightness
- Persistent symptoms
- Pathologic damage
(even when symptoms are not present)

Characteristic Features of Asthma Inflammation

- Mast cell activation
- Inflammatory cell infiltration
- Edema of the airway
- Denudation and disruption of bronchial epithelial smooth muscle
- Collagen deposition beneath the basement membrane
- Goblet cell hyperplasia with mucus hypersecretion
- Smooth muscle thickening

Adapted from: Pediatric Asthma: Promoting Best Practice, a Guide for Managing Asthma in Children. American Academy of Allergy, Asthma & Immunology (1999); reviewed by Asthma Ready® Communities Staff (2010).

DEFINITION OF ASTHMA

National Heart Lung and Blood Institute Expert Panel Report 3, (2007) defines asthma as:

.. a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular, mast cells, eosinophils, T lymphocytes, neutrophils, and epithelial cells. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night and in the early morning. These episodes are usually associated with wide spread but variable airflow obstruction that is often reversible either spontaneously or with treatment. The inflammation also causes an associated increase in the existing bronchial hyperresponsiveness to a variety of stimuli. Reversibility of airflow limitation may be incomplete in some patients with asthma (NHBLI, 2007, p. 14).

Pathogenesis of Asthma

Inflammation

- Found in patients with mild, moderate and severe asthma
- Common airway infiltration by inflammatory mediators
- Mast cell degranulation common with mild and moderate persistent asthma
- Epithelial denudation and deposition of collagen to the basement membrane can occur in severe (and often fatal asthma) mucus may occlude the bronchial lumen; bronchial smooth muscle may become hypertrophied; goblet cell hyperplasia may occur.
- IgE antibodies involved with severity of asthma, especially in early airway response to allergens
- Existing allergic illness is a major risk factor for the pathogenesis of asthma.
- IgE antibodies bind to mast cells and basophils, signaling the release of histamine and various leukotrienes, resulting in rapid constriction of airway smooth muscle.
- Mast cells produce various cytokines, contributing to both acute and chronic inflammation.
- Asthma treatment is focused on controlling underlying airway inflammation.

Immune Factor Involvement

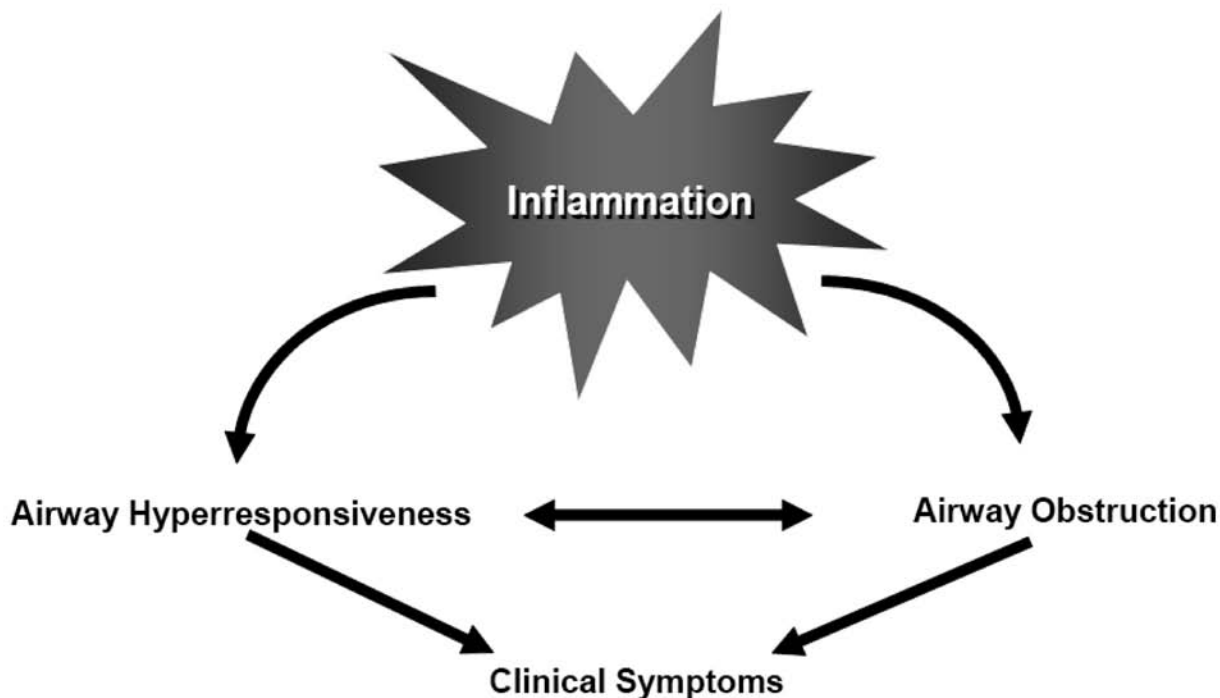
- An imbalance occurs between T-helper cells Th1 and Th2.
- Airway inflammation may represent loss of balance between opposing types of T-helper cells.
- Environmental exposure to certain antigens by children genetically capable of generating IgE antibodies may contribute to the development of asthma.
- New treatments being generated to treat leukotriene activity in allergic asthma.
- Interrelationship between immune factor development and airway inflammation

*Source: National Asthma Education and Prevention Program
Expert Panel Report (2007), National Heart Lung and Blood Institute, as printed in the
Journal of Allergy and Clinical Immunology, November 2002. Reviewed by Asthma Ready® Communities Staff (2010).*

KEY DIFFERENCES FROM 1997 AND 2002 EXPERT PANEL REPORTS

- The critical role of inflammation has been further substantiated, but evidence is emerging for considerable variability in the pattern of inflammation, thus indicating phenotypic differences that may influence treatment responses.
- Gene-by-environmental interactions are important to the development and expression of asthma. Of the environmental factors, allergic reactions remain important. Evidence also suggests a key and expanding role for viral respiratory infections in these processes.
- The onset of asthma for most patients begins early in life with the pattern of disease persistence determined by early, recognizable risk factors including atopic disease, recurrent wheezing, and a parental history of asthma.
- Current asthma treatment with anti-inflammatory therapy does not appear to prevent progression of the underlying disease severity.

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



Retrieved from Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma (2007)