Childhood Asthma—Advances in Pathogenesis

N. Somu, N.C. Gowrishankar, L. Subramaniam, D. Vijayasekaran, B.M. Muhajir and A. Balachandran

Department of Pediatric Respiratory Diseases, Institute of Child Health & Hospital for Children, Madras.

Abstract. Increase in morbidity and mortality of asthmatics in the world is a cause of concern. Many researchers have described various aspects of etiopathogenesis which has thrown light on the better understanding of asthma. Our experience with nearly 3 lakhs of asthmatic children, over a period of twenty-five years and our studies in Asthma clinic of ICH & HC, Madras generated new ideas to propose a hypothesis on etiopathogenesis of asthma. "Asthma is a disease caused by a specific infective agent in a genetically predisposed individual resulting in altered cellular response initially leading to hyperactive bronchial tree which on exposure to various aggravating factors manifest clinically as recurrent cough, dyspnoea and wheeze". Category of wheezers who manifest asthma is also discussed. (Indian J Pediatr 1996; 63 : 25-36)

Key words: Etiopathogenesis; Asthma; Pathogenesis.

In the recent years, asthma has received wide attention throughout the world because of increasing morbidity and death rate.1 The factors responsible for this apparent increase in the severity of asthma remain unclear. Underuse of anti-inflammatory agents, environmental pollutants, inadequate assessment of worsening airflow obstruction by patient and physician, lack of access to medical care, and non-compliance with prescribed therapy have been implicated in the recent rise in asthma mortality and morbidity.2,3

For many decades the basic mechanism of asthma was thought to be due to bronchial obstruction following bronchial spasm, mucosal edema and mucus hypersecretion. Technological advances in the medical field such as fiberoptic bronchoscopy, electron microscopy, immunocytochemistry have made researchers and clinicians to change their view. Presently, it has strongly been believed that the increased airway responsiveness in asthma is due to underlying chronic persisting inflammation demonstrated by cellular infiltration of the bronchial mucosa and submucosa by eosinophils and other inflammatory cells.

The purpose of this article is to summarise available information to provide a comprehensive idea of the pathogenesis of asthma and to project our newer hypothesis.

Airway Hyperresponsiveness

Airway obstruction is the result of underlying propensity of the airways to con-
strict. This concept is referred to as airway hyper-responsiveness and considered a central feature of asthma. The level of airway hyper-responsiveness in normal children is related to the age; with normal infants and young children being more responsive to methacholine than older children. Viral infection is believed to be an important cause of asthma exacerbations in children. Although the precise mechanism is not known, induction of airway hyper-responsiveness is believed to occur due to the ability of viral pathogens to produce an inflammatory process within the airways as a result of an infectious process. The increased airway hyper-responsiveness as a result of viral infection may persist for days or weeks after infection. The degree of airway hyperresponsiveness correlates with asthma symptoms. Patients with mild chronic asthma have fewer symptoms and have lesser degree of airway hyperresponsiveness. The patients with moderate severe asthma have more persistent symptoms and have a high degree of airway hyperresponsiveness. Patients with severe chronic asthma have almost daily symptoms and have an exaggerated airway hyperresponsiveness.

Atopy

Exposure of atopic individuals to allergens can lead to an increase in airway responsiveness that persists for days, weeks or months. It has been described that a vicious cycle can develop in which continuous or repeated exposure to allergens in allergic individuals insidiously leads to increased airway responsiveness. Subsequent exposure to allergens or non-allergic stimuli may then more easily lead to airway obstruction. Thus stimuli encountered in environment that do not normally produce symptoms (exercise or smoke) now produce symptoms. Allergen exposure leads to an inflammatory reaction within the airways that is associated with changes in airway function (obstruction and increased responsiveness). The inflammation and increase in responsiveness appear to be the greatest when allergen exposure leads to an immediate asthmatic response within minutes of exposure and late asthmatic response hours later.

Airway Inflammation

The presence of airway inflammation in all subjects with asthma indicates that this inflammatory process is the key factor in the development of airway hyperresponsiveness. Knowledge in this area may lead to new avenues of treatment. The role of underlying airway inflammation in asthma is undisputed. The inflammation could be due to release of toxic substances from inflammatory cells, as widely reported or could be due to infection.

The epithelial cells participate in several ways in the pathophysiological mechanisms of asthma. The shedding of ciliated epithelial cells from the basal cells may be due to mediators released from inflammatory cells. The loss of bronchial epithelium denudes nerve and mast cells and increases the reactivity of smooth muscle cells. Increased thickness of basement membrane is also reported. The bronchial submucosa often shows edema, vasodilation and mixed cellular infiltrate. Bronchial smooth muscle hypertrophy and hyperplasia support the view that bronchial smooth muscle shortening and thickening of the wall contribute to narrowing of bronchial lumen.