

# EDITORIAL

## BRONCHIAL ASTHMA - PROBLEMS AND CHALLENGES

The prevalence of bronchial asthma, a major public health problem is increasing world wide (1,2). Asthma was found to be more prevalent among black and poor American children (3). However, other studies had not shown such racial differences (4,5). High prevalence of asthma has been reported in urban areas and low prevalence in rural communities (3,6). prevalence of asthma is also found to be higher in boys than in girls (7). Other risk factors for developing asthma especially in children include exposure to environmental tobacco smoke and air pollution, low birth weight, and children of younger mothers (8). Several studies had demonstrated increase in morbidity and mortality from bronchial asthma (9). Over and under treatment of asthma may be responsible for high mortality rates (10). The increase in asthma deaths has been attributed to regular use of  $\beta$  agonists that may lead to worsening of asthma (11). The excess mortality from  $\beta$  agonists has been demonstrated with fenoterol but not with salbutamol (11,12). However, further long term studies are required to settle this controversy. India is a subcontinent with different geographic, racial, cultural and economic groups. It is a pity that there are no well conducted studies from India to know the exact prevalence of asthma and its influence on various geographic, socio-economic and racial factors. In this issue of the journal, Gupta provides the clinical profile of the asthma as seen in eastern India (13). Even though it is a hospital based study, it gives a glimpse of the gravity of the problem. Therefore, there is an urgent need for undertaking multicentric prevalence studies in bronchial asthma in our country.

Until recently bronchospasm that results from hyperresponsiveness of the lower airways to a multiplicity of stimuli has been regarded as the main cause of airway dysfunction in asthma. However, postmortem findings in the airways of subjects dying of acute asthma had shown widespread infiltration of inflammatory cells especially lymphocytes and eosinophils, desquamation of epithelial cells and mucus hypersecretion (14). Subsequently, studies utilising both bronchial biopsies and bronchoalveolar lavages have identified cellular infiltrations of the bronchial mucosa and submucosa by eosinophils and other inflammatory cells even in patients with mild stable asthma (15,16). Thus airway inflammation is found in both fatal and mild forms of asthma. Based on these studies, bronchial asthma is now defined as a chronic persistent inflammatory disease of the airways (2). Electron microscopic,

immunohistochemical and molecular biological techniques used in the study of the cells and mediators in the samples obtained by biopsies and lavages have enabled us to better understand the immunopathogenesis in bronchial asthma. Salvi and Holgate have described in detail the recent developments in immunopathogenesis of asthma in this issue (17). Multiple cytokines have been implicated in asthma and they are derived from a variety of cells including epithelial cells. Future studies may unravel the role of epithelial and endothelial barriers in regulating inflammatory chemotactic responses including the role of adhesion molecules. Studies are required to define the role of inflammation in nocturnal asthma as conflicting results are obtained in nocturnal asthma by BAL studies (18,19). Respiratory infections commonly with viruses can precipitate symptoms of wheezing in patients with asthma especially in children and can induce airway hyperresponsiveness in non-asthmatics (20,21). However, the mechanism responsible for those reactions following viral infections are not clear. Studies are also essential to know how a single massive exposure to irritant gases such as that occurred at Bhopal causes asthma - like syndrome termed as reactive airways dysfunction syndrome (22,23). Another area that requires in depth study is the role of genetics in asthma as it has been demonstrated that there is an increased frequency of asthma and / or hyperresponsiveness in first degree relatives of asthmatics (24).

The realization that inflammation is the key factor in the pathogenesis of asthma, is reflected in the recent trend in asthma therapy with emphasis on anti-inflammatory drugs (2). Glucocorticosteroids are the most potent antiinflammatory agents available for the treatment of asthma. The systemic side effects of corticosteroids can be reduced by delivering the drug by inhaled route. Efficacy of inhaled glucocorticosteroids can be enhanced by using a large volume spacer device. Beclomethasone dipropionate, budesonide, fluticasone propionate, triamcinolone acetonide and flunisolide are available as inhaled glucocorticoid preparations. Sodium cromoglycate and nedocromil sodium are other anti inflammatory drugs. Inhaled corticosteroids upto 1000 ug per day may not cause adrenal suppression in adults (25). However, in children, doses between 400 and 800 ug daily may retard growth. Fluticasone propionate is a novel inhaled glucocorticoid with an improved efficacy and safety profile compared to currently existing inhaled

steroids (26). Fluticasone has the added advantage that it has negligible oral bioavailability and hence unlike beclomethasone and budesonide, there is little or no systemic effect from swallowed portion of the drug (26). However studies using this drug are required to assess the safety profile in Indian patients. Some patients with chronic severe asthma may require long term oral maintenance treatment with steroids resulting in steroid toxicity. Role of drugs such as low dose methotrexate and cyclosporin is being evaluated in treatment of such corticosteroid dependent asthmatics (27,28). In this issue of the journal, Bedi gives an account of methotrexate in the treatment of steroid dependent asthma (29). However, these drugs should be used with caution under strict supervision of a chest specialist.

Treatment of bronchial asthma with immunotherapy is controversial (30). There are only a few well conducted studies to critically evaluate the usefulness of immunotherapy. Even though there is a possibility that immunotherapy may block allergeninduced inflammation, there are no proper studies using BAL and bronchial biopsy to prove this hypothesis. New drugs that are under development for the treatment of asthma include VIP/VIP analogues, selective phosphodiesterase (type III, IV, V) inhibitors, potassium channel openers, calcium antagonists, nitrodilators (nitroprusside, atrial natriuretic peptide), selective anticholinergics ( $M_3$ -antagonists), mediator antagonists (antagonists to leukotriene D<sub>4</sub>, 5-Lipoxygenase and platelet activating factors), cytokine inhibitors (IL-5 inhibitor), IgE suppressors (IL-4 inhibitors), inhaled frusemide, cell adhesion blockers, immunomodulators (cyclosporin A, FK 506, rapamycin) etc (31). As n-3 fatty acids in fish oil inhibit prostaglandin and leukotriene production from arachidonic acid, there is a suggestion that fish oil may be useful in the treatment of asthma (32,33). However, the role of dietary fish oil in asthma is not yet proved (33).

Many National Thoracic societies have formulated consensus reports for treatment of asthma (2,30). In a country like ours, the long-term management of asthma with inhaled corticosteroids and  $\beta$  stimulants is difficult because of high costs and lack of patient education. Role of cheaper drugs like theophylline should be defined especially in our country. Therefore, we should develop recommendations for management of asthma keeping in mind the socioeconomic condition and literacy of patients. Finally the question that is being asked by many Patients for which we do not have an answer at present is : can asthma be cured ? Let us hope that research in bronchial asthma may ultimately lead to a cure in asthma.

**VK Vijayan**

Cardio-Pulmonary Medicine  
TRC, ICMR, Madras 600 031.



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## ANNOUNCEMENT

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#### THE AMERICAN COLLEGE OF CHEST PHYSICIANS

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Dr VK. Vijayan

Organising Chairman

Cardio-Pulmonary Medicine

TRC, ICMR, Madras 600 031.

**Telephone:**

(044) 8265425 (7 - 16 hours)

(044) 423234 (17 -22 hours)

**Fax:**

(044) 8262137

**E mail:**

icmrtrc @ ren.nic.in