

CORRELATION BETWEEN ASPERGILLUS PRECIPITATE IN BRONCHIAL
ASTHMA AND VENTILATORY FUNCTION TEST

THESIS
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INTRODUCTION

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Aspergillus fumigatus and less frequently species of *Aspergillus* caused allergic disease in sensitized persons. (Argarbrit J. W. et al., 1963).

Exposure to *aspergillus* conidia might be followed promptly by either asthmatic attacks or broncho-Pulmonary infiltrations. (Assem et al., 1974).

The presence of anti-fungal antibodies especially precipitin was indicative of previous exposure to the antigen or a recent infection, if the reaction is strong or titre is rising, an active infection could be suggested. (Droughor et al., 1963).

The Aim of the Present work :

is to search for precipitin antibodies in serum for *aspergillus* species and test the correlation between the number of precipitin lines and ventilatory function tests in different types of bronchial asthma.

REVIEW

BRONCHIAL ASTHMA

Asthma is a disorder that is characterised by increased responsiveness of the trachea and bronchi to various stimuli, resulting in widespread narrowing of the air ways.

Most asthmatic patients are diagnosed by a triad of episodic symptoms : wheezing, cough and dyspnea. Characteristically these signs are highly variable in severity and duration.

They may run the gamut from being completely absent for days, months, and even years to being protracted and unresponsive to outpatient therapy. [status asthmaticus] .

Asthma is frequently classified according to its course or in term of frequently seen patterns, and patients will fall into more than one of the usually defined groups (Druce, 1985).

1. Extrinsic asthma :

The extrinsic form of asthma accounts for less than ten per cent of all patients. This group has a frequent family history of asthma, seasonal variation, childhood onset and a well - defined allergic history to a variety of inhaled allergens (atopy).

They have positive skin tests with a typical wheal and erythematous reaction confirming the presence of type I cell

review (2)

and immunological reaction as serum IgE is the major component of their asthma (Druce, 1985).

2. Intrinsic asthma :

These asthmatics have no known external allergens, skin testing tends to be negative and IgE is normal or low. Intrinsic asthma usually begins after the age of 30 and tends to be perennial and more severe. Blood and sputum eosinophilia are common in both extrinsic and intrinsic asthma (Druce, 1985).

More than 80% of asthmatic patients have clinical features that are common to both groups.

3. Cough induced asthma :

A form of asthma in which the only manifestation is cough, with similarity in history and other findings to intrinsic asthma.

Asthma was found to be the sole cause of chronic persistent cough in 25% of cases of chronic cough (Irwin 1981). Cough responds dramatically by atropine.

4. Occupational asthma :

A variety of occupational dusts and fumes may provoke asthmatic attacks in susceptible individuals. Both allergic and irritant stimuli are thought to be involved in occupational asthma. Important diagnostic clues include a cyclic pattern in which symptoms-free periods occur during week ends or vacations.

5. Exercise induced asthma :

In some patients, exercise may also induce broncho spasm. there are two hypotheses to explain how broncho spasm is induced.

One implicates mainly heat transfer from the respiratory tree; the other proposes that it is respiratory water loss, resulting in an increase in the osmolarity of the epithelial lining fluid (Anderson 1984).

The chemical mediators of immediate hypersensitivity may produce this type of asthma by acting directly on air ways smooth muscle, by directly triggering neurogenic reflex or by activating circulating neutrophils (Papa gearigou, 1983), supporting this view is that cromolyn or beta 2 drugs and calcium channel blockers can prevent exercise induced asthma (Chand. 1985).

Aspirin induced asthma :

In about 10% percent of asthmatic patients, a peculiar triad exists of bronchospasm, nasal polyps, and sensitivity to aspirin. Ingestion of aspirin, and/or indomethacin may induce bronchospasm, urticaria and even hypotension. The reaction is not immunologic but due to abnormality in prostaglandin metabolism by the inhibition of cyclo-oxygenase pathway, diversion of arachidonic acid metabolism toward the lipoxyg- enase pathway and the production of spasmogenic Leukotrienes.

Pathophysiology of Extrinsic asthma :

Inhaled allergens interact with specific IgE antibodies that are fixed to mast cells that line the tracheobronchial tree. Mast cells and possibly basophils that are sensitized with IgE are primed to respond to specific allergens when cell-bound IgE is bridged by divalent allergen. This membrane event signals mast cells to secrete a variety of mediators leading to opening of tight junctions between epithelial cells lining the airways, thereby facilitating an ingress of additional antigens into the mucosa (Waserman. 1983).

Mediators are of 2 kinds, either preformed which are contained in metachromatic granules of mast cells and released by a process of exocytosis. Important examples of these mediators are histamine, eosinophilic factors of anaphylaxis and neutrophil chemotactic factor. the other kind of mediators are unstored and secreted by mast cells within minutes after antigen stimulation. these mediators are leukotrienes, platelet activating factors and prostaglandins (PGD_2 and $PGF_2 \alpha$) .

Grantja and Lichtenstier (1974) demonstrated that human leucocytes from atopic donors stimulate and secrete leukotrienes on sensitization with pollen antigens or anti IgE. They are synthesized from the 20 carbon unsaturated. Fatty acid, arachidonic acid. Arachidonic acid is derived

from cell membrane phospholipids by the action of phospholipase and is converted via lipoxygenase and cyclooxygenase (Palmer and Solman 1983). The former leads to the formation of leukotrienes which have a potent chemotactic factor for eosinophils and neutrophils (LTB_4) and smooth muscle contracting properties (LTC_4 , LtD_4 , LTE_4).

The leukotrienes are a thousand times more potent on a molar basis than histamine or $PGF_{2\alpha}$ and exert their effect predominantly in the distal or small air ways.

In asthmatic patients allergens induce the release of leukotriene C_4 , D_4 or E_4 from lung tissue that correlate well with their capacity to induce bronchial contraction (Barnes, castello JF, 1984).

Secretion of primary mediators initiates the release of secondary mediators, such as serotonin, prostaglandins and possibly kinins. the effects of these mediators may be viewed as two waves of an inflammatory response:

The first is an immediate transudation caused by increased capillary permeability. The second occurs hours to days after antigen stimulation and involves the accumulation of inflammatory cells (Late - onset asthmatic response).

The late onset of the airways is associated with an accumulation of neutrophils, platelets, and eosinophils in the bronchial mucosa and submucosa.

The reaction is initiated by mast cells and basophils via secretion of mediators followed by the arrival of neutrophils to elicit the infiltration of mononuclear cells in the sub-mucosa, which may persist for several days (Ka Liner MA 1985).

Pathophysiology of intrinsic asthma :

In intrinsic asthma, reversible air ways obstruction is caused by a variety of stimuli that are non antigenic and seemingly unrelated.

Intrinsic asthma represents an abnormality of the parasympathetic nervous system where bronchospasm is provoked via stimulation of rapidly adapting irritant receptors which are located in the subepithelial region of the tracheobronchial tree (Sheppard D. 1986).

Impulse from these rapidly adapting irritant receptors are carried by the afferent vagal fibres; the reflex arc is completed by efferent vagal fibres, which innervate bronchial smooth muscle and cause bronchoconstriction (Nadel JA, Barnes D J, 1985).

The late onset reactions may be involved in the interaction between mediator release and neurogenic stimuli as an important feature of the late onset is an increase in airway hypersensitivity. It is likely that the infiltration of the bronchial mucosa with inflammatory cells

and continued release of mediators further stimulate irritant receptors.

IMMUNE EFFECTOR CELLS IN ASTHMA

(1) Mast cells :

Lung mast cells are most abundant in the membranous portion of trachea, beneath the pleura and in the connective tissue surrounding small airways and blood vessels. The classic mast cell-secretory reaction is triggered by allergens that bridge specific IgE antibodies associated with mast cell on basophils - IgE Fc receptors. This initiates a secretory reaction with the discharge of granules which in lung cause asthma. Secretion by mast cells and basophils is regulated by two classes of membrane receptors; those that activate adenylate cyclase to produce cyclic adenosine. 3',5' monophosphate (cyclic AMP) and those that stimulate guanylate cyclase to form guanosine. 3',5' monophosphate (cyclic GMP).

Two additional receptors have also been shown to stimulate adenylate cyclase: histamine (H₂ type) and prostaglandin (PGE receptors).

These receptors provide some evidence for a negative feedback control mechanism for mast cells and basophils.

The transient increase of cytoplasmic cyclic AMP inhibits the release of histamine, SRS.A and other mediators, but in contrast, guanylate cyclase stimulates the formation of cyclic GMP which enhances mediator release.

It was found that the best studied receptor that activates adenylate cyclase is the beta receptor and acetylcholine stimulates the production of cyclic GMP.

Now it has been proposed that asthma results from a partial blockade of beta receptor, leading to an imbalance between the inhibitory (cyclic GMP) and excitatory (cyclic AMP) messenger molecules regulating mediator release.

(2) Role of esinophils and neutrophils :

The esinophils and neutrophils paly a prominent role in the late onset reaction especially in their capacity to inflict injury. Granular constituents derived from the eosinophil, particularly major basic protein, and the secretion of oxygen free radicals can injure bronchial epithelial cells, rendering the mucosa more permeable to allergens, and possibly lowering the threshold of underlying irritant receptors (Fillery 1982).

Eosinophils can also generate LTC₄ and toxic oxygen metabolites. Similarly Neutrophils and macrophages can release lysosomal enzymes free oxygen radicals (Parson 1984)