THE ROLE OF MOLD FUNGI IN THE AETIOLOGY OF BRONCHIAL ASTHMA

THESIS

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BY

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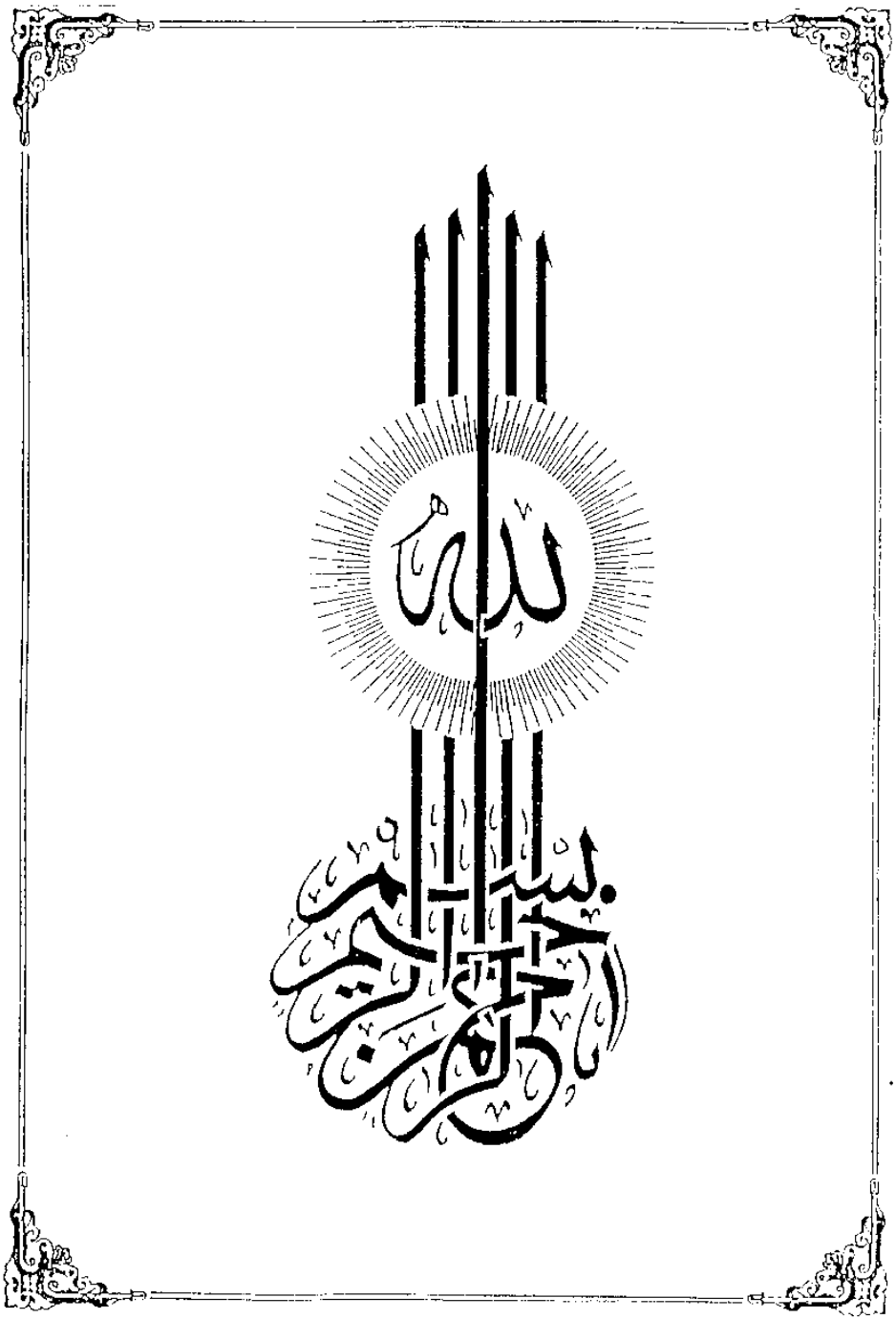

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INTRODUCTION
and
AIM OF THE WORK

INTRODUCTION AND AIM OF THE WORK

Bronchial asthma is a disease which may be caused by various allergens which are dispersed in the environment. Detection of these allergens in many cases may help in the control of the disease .

The possible role of molds as allergens in bronchial asthma was stressed by many investigators and it has long been recognized that inhalation of fungal fragments can produce allergic symptoms in susceptible individuals . Both upper and lower respiratory symptoms have been reported, but the actual prevalence of asthma resulting from inhalation of mold spores and/or mycelial fragments is not known (Lehrer et al., 1983) .

Fungus spores can act as an excitent and can have an etiological role in some cases of bronchial asthma either in initiating or aggravating the conditions and may be complicated by allergic pulmonary infiltrations . However , fungi may be present as saprophytes in the bronchi .

The aim of this work is to search for molds in the sputa of asthmatic patients fungal spora of their homes and its precipitins in their sera . Skin tests for molds will also be done and a trial to correlate these findings with their bronchial asthma will be considered .

REVIEW OF LITERATURE

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Bronchial Asthma

Bronchial asthma has been known since 2000 years (Rosenblat , 1976) .

In 1967, The United States National Tuberculosis Association produced the definition : Asthma is a disease characterized by an increased responsiveness of trachea and bronchi to various stimuli and made manifest by difficulty in breathing and generalised narrowing of air-ways . The basic defect appears to be an altered state of the host (Pepys , 1973) .

Asthma has also been defined as a disease characterised by wide spread variation over short period of time in resistance to flow in the airways. It may be related to exposure to environmental factors specially inhaled substances or thay may occur without apparent external cause .

Among the detectable factors, are specific antigen antibody reaction to inhaled allergen, and hyperreactivity of the airways to various chemical and physical stimuli and to exercise. The resistance will decrease by bronchodilator drugs and corticosteroids (Scadding et al., 1976) .

Bronchial Hyperreactivity

Bronchial hyperreactivity is a condition in which the airways show a much greater bronchoconstrictor response to provocation stimuli than normal . The stimuli may be specific as house dust allergens, or non specific such as exercise, inhalation of cold air or a variety of irritants and pharmacological agents .

Non specific bronchial hyperreactivity is a feature of asthmatic patients both allergic and non allergic (Nadel and Pauwels, 1982) .

The control of airway smooth muscle is far more complex than was though 5 - 10 years ago . There is a vagal cholinergic motor pathway, excitation of which causes bronchoconstriction . In addition, bronchodilator mechanisms are present and may involve both adrenergic and non-adrenergic pathways . The activity in all these pathways is by activation of parasympathetic neurones .

II. Infection :

Patients with chronic bronchitis have greater tendency to airways obstruction after viral or bacterial respiratory infection than infection free periods. Proteolytic enzymes released by bacteria or leukocytes, sensitize the parasympathetic receptors of airways (Ulmer, 1979).

III. Non specific bronchial hyperreactivity stimuli :

Mechanical, thermal and chemical stimuli can irritate bronchial system; they increase the rate of bronchial musculature, via vagal reflex action induced by release of acetyl choline (Nadel, 1982) .

IV. Inflammation and bronchial hyperreactivity :

Inflammatory agents are important causes of bronchial hyperreactivity . They alter the permeability of tight junctions between the epithelial cells of mucous membrane may respond abnormally to produce symptoms and signs of bronchoconstriction, cough, secretory abnormalities and wheezes .

Exogenous factors causing bronchial hyperreactivity :

I. Allergy :

It is the commonest exogenous mechanism of bronchial hyperreactivity. In atopic patients, antigens induce formation of IgE antibodies, which attach themselves to the surface of tissue mast cells and of basophilic leukocytes in the blood . This provokes the immediate release of mediators such as histamine , slow reacting substances of anaphylaxis and leukotriens . This provokes acute airway obstruction.

This occurs infrequently in non-atopic subjects in whom an IgG acts as an antibody (Gell and Coomes, 1968).

Nadel (1973) suggested that a part of mediator action is modulated by central nervous system . This receives input both from receptors in the airways and from elsewhere. Many different reflexes cause changes in bronchomotor tone and other factors such as cough, ventillation, laryngeal caliber and mucous secretion; such changes are known to be a part of bronchial hyperreactivity (Widdicombe, 1982).

Mechanism of airway hyperreactivity :

Asthma has been thought to be an IgE mediated disease associated with the release of mediators from mast cells in the lung . Asthmatics have elevated responsiveness to mediators such as histamine .

Administration of such compounds cannot induce asthma in healthy person . Many types of cells are present in the airways, such as gland cells, ciliated cells receptors, nerves and muscles . In asthma, all of these cells are lining the airways . This effect leads to bronchoconstriction reflexly, by stimulation of receptors protected by such junctions (Nadel, 1982) .

Recently, the trypase enzyme has been known to constitute at least one-third of proteins in human lung mast cells . It causes breaking down of tight junction and consequently increased bronchial reactivity (Empey, 1982).

V. Smooth muscle abnormality and bronchial hyperreactivity:

The smooth muscles appear to be abnormal in asthma and chronic bronchitis. Hypertrophy and hyperplasia of airways smooth muscles are among the major pathological changes in asthma and chronic bronchitis (Nadel , 1982) .

VI. Calcium ions :

Errors in calcium ion regulation could lead to bronchial hyperreactivity as calcium ions involved in regulation of many cellular processes including smooth muscle contraction. So, calcium antagonists may be helpful in reduction of bronchial hyperreactivity (Triggle, 1982) .

VII. Prostaglandins :

Prostaglandins seemed to play little part in control of airways smooth muscle tone. They are involved in induction of airway hypersensitivity in mild asthmatics and control of airways reactivity. Chronic B-adrenergic stimulation of airways induced changes in the sensitivity dependent upon prostaglandin production (Walters , 1982) .

Biochemical Mediators In Asthma

Chemical mediators have been suspected to have a part in the pathogenesis of asthma . The central role of lung mast cells as a source of mediators include basophils, other free cells within the lung and site distant from the lung . Mediators act in a number of ways, directly on the tissue of airway and lung, and indirectly via reflex mechanism and by recruitement of the inflammatory cells including neutrophils and oesinophils .

Recent evidences suggested that hyperreactivity of the airway in asthma may not be a generalised disorder affecting all elements in the airway, but rather a response of a specifically located contractile elements reacting to diverse groups of agonists and irritants (Griffin et al., 1983) .

Two main classes of mast cell mediators have been recognised, preformed mediators contained in granules with the cytoplasm and other derived from the cell membranes.

1. Mast cell granule mediators :

The cytoplasmic granules of human mast cells have been shown to contain histamine, a number of polypeptide constituting the oesinophil chemotactic factor of anaphylaxis(ECFA),

high molecular weight neutrophil chemotactic factor (HMW. NCF) and a number of neutral proteases, acid hydrolases and heparin proteoglycan . In man, histamine is stored within mast cells and basophils . Many individuals with asthma challenged with specific antigen or exercise show a rapid rise in the airway resistance associated with a variable increase in plasma histamine concentration (Barnes and Brown, 1981 and Lee et al., 1982) .

Mast cells degranulation leads to classical allergic reactions appearing within minutes and abating in 30 - 60 minutes . It is now appreciated that this is the first stage of multisequenced reaction that induces the later phase allergic reactions that are apparent within 4 - 8 hours and persisting up to 24 hours . This late phase reactions (LPR) are clinically experienced as burning , ill defined erythema and oedema and are thought to participate in airway and nasal hyperreactivity (Kaliner and Lemauske, 1984) .

2. Mast cell membrane mediators :

A number of potentially active chemical mediators may be relevant specially to the inflammatory component of asthma and derived from cell membrane precursor notably arachidonic acid (Ishizaka et al., 1980) . The arachidonic