BRONCHIAL CHALLENGE IN ASTHMATICS WITH ASPERGILLUS ANTIGEN

THESIS

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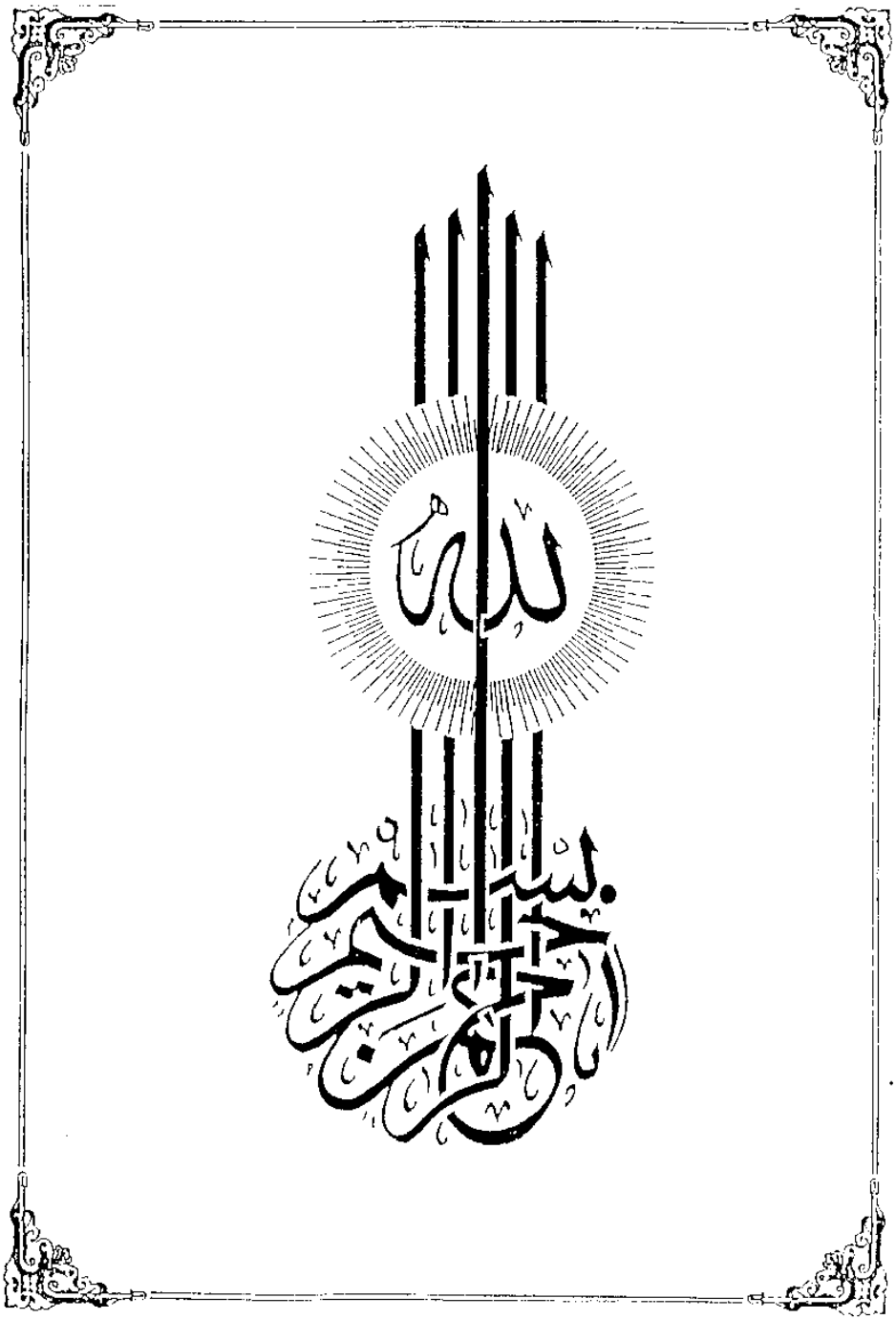

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C O N T E N T S

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INTRODUCTION AND AIM OF THE WORK

The inhalation test with specific allergens is the most accurate method of determining clinical sensitivity in asthmatic subjects although its use is still largely experimental.

Bronchial provocation tests that are carefully performed by experienced investigators can yield much information of etiologic and therapeutic values.

Asp. fumigatus is the most virulent antigen of all aspergilli as far as respiratory disease is concerned.

In Egypt, the study of bronchopulmonary mycosis did not receive enough attraction. This may be due to that bronchopulmonary mycosis was thought to be more or less rarer in Egypt than in other some countries. Also, the diagnosis needs special laboratories and special techniques which are not available.

In 1977, Ain Shams mycology laboratory was installed by the staff of chest medical department. They are searching for the entity of bronchopulmonary mycosis.

Testing the bronchial reactivity to inhalation of Asp. fumigatus antigen appears to be a logical approach to evaluate the immediate and late reaginic bronchial reaction to the Asp. fumigatus antigen.

The aim of this study is to detect the presence or absence of bronchial reactivity in asthmatics and to assess the effect of inhalation of Asp. fumigatus antigen on pulmonary ventilatory function tests.

REVIEW OF LITERATURE

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Bronchial Hyperreactivity

Normal subjects may inhale a variety of irritants such as smoke, sulph.dioxide, dusts and, in certain concentrations, aerosols of pharmacological agents such as histamine, carbachol or methacholine with little or no change in airways resistance. By contrast, subjects exist in whom inhalation of these agents promptly provoke bronchoconstriction with tightness, breathlessness, and often coughing, i.e. they exhibit bronchial hyperreactivity. The most sensitive individuals are usually patients with the clinical syndrome of asthma, but some patients with chronic bronchitis and airway obstruction in whom there is no evidence of allergy are also hyperreactive (Stretton, 1976).

The mechanism of hyperreactivity is uncertain, but the ability of isoprenaline to reverse rapidly the changes strongly suggests that constriction of bronchial muscle is the dominant reaction. Whether bronchoconstriction is due to direct effect of the agent upon the tissues or due to a reflex response mediated by the vagi is also uncertain and there is evidence that either or both mechanisms may exist (Stretton, 1976).

Benson (1975) has adduced evidence that at least a part of bronchial hyperreactivity is a consequence of bronchoconstriction and of increased bronchomotor tone.

There are variations in the degree of reactivity within any particular subject under certain conditions. There is diurnal variation. Bronchial responsiveness is greatest at night, the time when pulmonary function is often worst. In patients with a tendency to asthma reactivity is greatest during or immediately after an attack of asthma and diminishes as there is clinical improvement (Benson, 1975). In normal subjects hyperreactivity is seen during or after a respiratory tract infection (Parker et al. 1965). Bronchodilator drugs tend to block or reduce reactivity (Benson, 1975).

Provocative Testing

Wherever doubt exists concerning the etiological relationship of a given allergen and an asthmatic paroxysm, the most valid test to establish the association is reproducing asthma with the specific allergen in question , by the route provoking the asthmatic attack (Weiss and Segal, 1976).

The inhalation test with specific allergens is the most accurate method of determining clinical

sensitivity is asthmatic subjects, although its use is still largely experimental (Aas, 1970).

Skin tests and bronchial reactivity do not always correlate because many reports include instances of strongly positive skin tests with negative bronchial reactivity, as well as of the reverse (Tse, 1972).

The over-all experience with inhalants showed that positive skin tests were associated with positive bronchial responses to the same allergen 61 percent of the time. In the case of challenges done in patients who were completely skin test negative, only 0.9 percent gave positive bronchial responses, and these were observed with a single allergen-house dust (Hyde, 1969).

The discrepancies between clinical histories and skin test reactions, and the disenchantment on the part of some physicians with the results of hyposensitization using allergens selected in large part on the basis of positive skin tests, have led to the search for other methods of diagnosis. Direct application of the suspected allergen to the shock organ is an old technique and one which received considerable attention in the United States and Europe during the period 1930 to 1955 (Schiller and Lowell, 1952).

The concentration of allergen required to elicit a positive skin test is much less than that needed to

obtain a positive bronchial challenge (Colldahl, 1952). Although the reason for this has not been established, it is probably related, in part, to the way of measuring end organ response. In some studies up to 80 per cent of the positive intradermal skin tests could not be confirmed by positive bronchial challenges (Bruce, 1963).

A technical limitation of bronchial provocation testing is that false positive bronchial challenges may be caused by nonspecific factors. For example, since hyperreactive airways are characteristic of the asthmatic patient, the effort of simply exhaling into a spirometer or inhaling the control solution may provoke airway narrowing (Hyde, 1969).

Bronchial provocation test is not carried out on patients with infections, pulmonary infiltrations, or signs of bronchial obstruction, though rhonchi heared on auscultation are ignored if lung function tests could be shown to be satisfactory. Patients who had corticosteroid medication recently, or antihistamines within 24 hours are not tested (Aas, 1970).

During the test the patient is observed. If cough or signs of nasal reactions, bronchial reactions, or changed respiration occur, nebulization is immediately stopped and the patient is examined more closely by auscultation and PEF measurements. If there

is any sign of bronchial reaction spirometry is also performed. The test is allowed to proceed if no convincing obstruction is found (Aas, 1970).

The most obvious drawback of bronchial provocation is its hazards. Moreover, provoking acute wheezing in previously asymptomatic subjects is unpleasant for both patients and their physicians. Despite these disadvantages, bronchial provocation tests that are carefully performed by experienced investigators can yield much information of etiologic and therapeutic value (Hinshaw and Murray, 1980).

If severe attack of asthma occurs, an injection of adrenaline is given and with antihistamines and theophylline preparation. Medication is continued for at least 12 hours (Aas, 1970).

With high concentration of antigenic extracts, a hypersensitization phenomenon may occur. However, progressively increasing the concentration of antigen makes hypersensitization unlikely and hyposensitization possible (Weiss and Segal, 1976).

Medication should be withheld prior to testing according to the following schedule: 6 hours for phosphodiesterase inhibitors, 6 hours for beta stimulators, and 24 to 48 hours for antihistamines. Since cromolyn sodium can inhibit immediate and dual asthmatic reactions,

and oral or inhaled corticosteroids can inhibit late reactions, they should also be withheld 24 to 48 hours (Pepys et al. 1974).

Since a fall in FEV_1 of greater than 20 percent can cause patient discomfort, we frequently give an aerosolized bronchodilator at the termination of a positive challenge. Accordingly, epinephrine and aerosolized bronchodilators should be on hand at all times while performing inhalation challenges (Weiss and Segal, 1976).

As soon as positive reactions are observed and registered, treatment is started with inhalation of nebulized isoprenaline 0,5% and with antihistamines, ephedrine and occasionally a theophylline preparation in that order (Aas, 1970) .

Results of inhalation provocation tests are quantitative and are influenced by a number of technical and nontechnical factors. The technical factors include the methods of aerosol generation and inhalation, of preparation and storage of test solutions, of measurement of the response, and of expression of results. Nontechnical factors include subject characteristics such as baseline airway caliber, medications and environmental factors such as time of day, respiratory infection and exposure to allergen (Ryan et al., 1981).