Quantitative Estimation Of Cholinesterase In Bronchial Biopsy In Patients With Bronchial Hyper-reactivity

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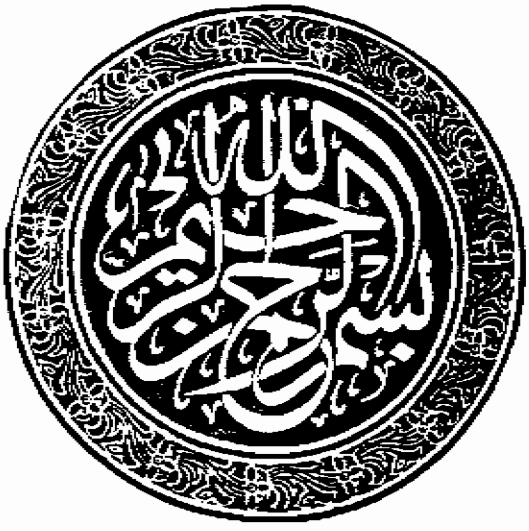

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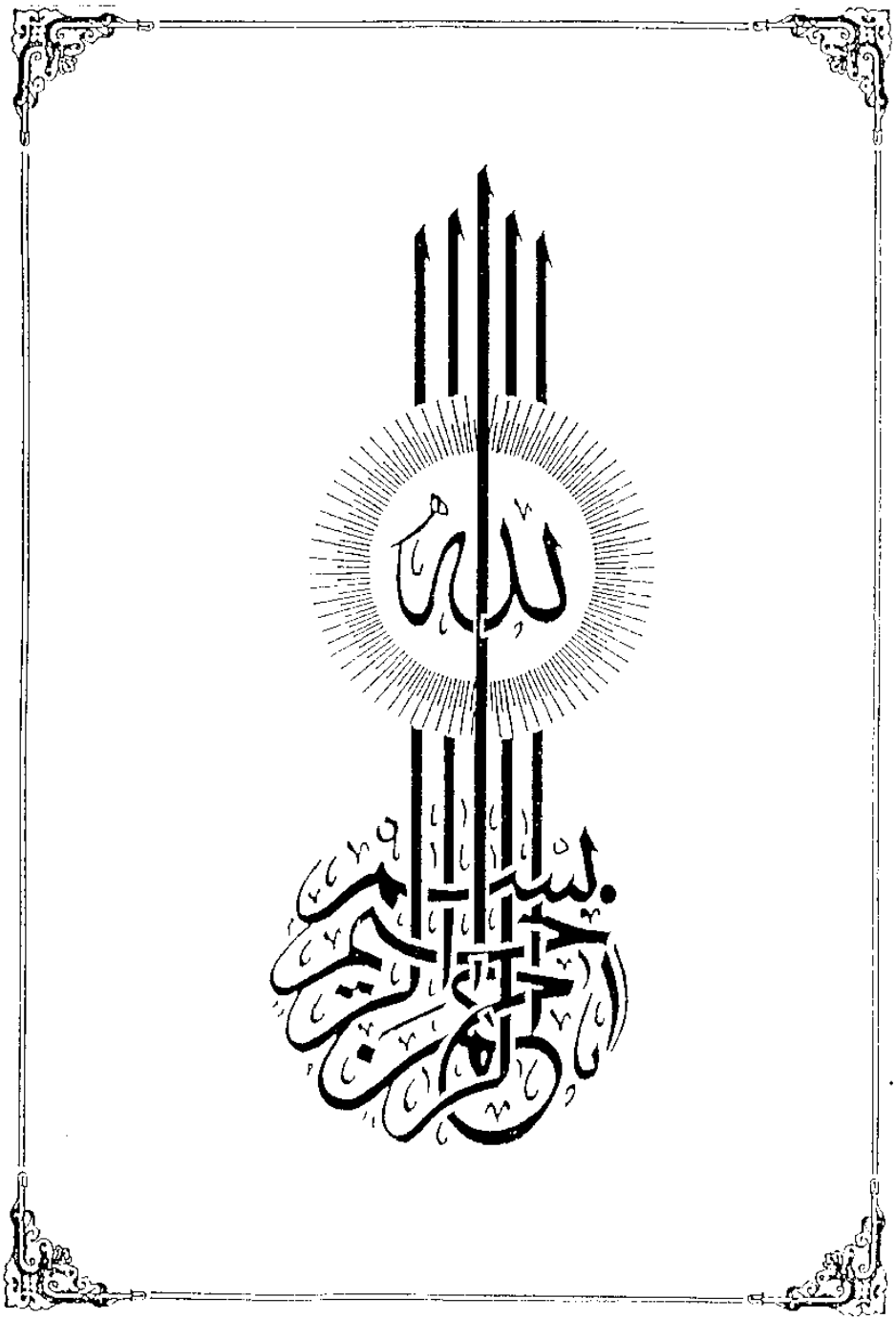

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INTRODUCTION AND AIM OF THE WORK

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Introdution and Aim of the Work

Bronchial hyper-reactivity is a condition in which the airways show an exaggerated bronchoconstrictor response to provocative stimuli. These stimuli may be specific (such as house dust mite allergens) or non-specific (such as exercise, inhalation of cold air) or a variety of irritants and pharmacological agents ***(Nadel and Pauwels, 1982)***.

Generalized obstructive airway disease (GOAD) is characterized by bronchial hyper-reactivity and several authors have described the possible mechanisms of bronchial hyper-reactivity. ***Nadel*** (1973) suggested that damage of the airway epithelium might play an important role in bronchial hyper-reactivity.

Benson (1975) mentioned that hypertrophy of the bronchial smooth muscle might be of importance inthe pathogenesis of bronchial hyper-reactivity (BHR). ***Richardson and Beland*** (1976) reported that disorders of the autonomic regulation might play an important role. These disorders may be in the form of increased either parasympathetic or alpha adrenergic activity or decreased either beta adrenergic or non-adrenergic inhibitory activity.

Boushey et al (1980) stated that bronchial hyper-responsiveness might be due to decreased baseline calibre. ***Goetzel*** (1981) stated that it might be caused by the mediators of the inflammation enhancing the responsiveness of the bronchial smooth muscles or their innervation. It

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may also be caused by chemotaxis of leucocytes by the inflammatory mediators.

Gomaa et al (1991) studied qualitatively the cholinesterase level in bronchial tissue biopsy in patients with GOAD and they found that there was absence of this enzyme in bronchial tissue in the majority of these patients, suggesting that there might be a role for this enzyme in the pathogenesis of bronchial hyper-responsiveness in patients with GOAD, and the aim of this work is to estimate the level of cholinesterase in bronchial tissue biopsy quantitatively in patients with bronchial asthma and to try to correlate the results with the degree of airway obstruction.

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REVIEW OF LITERATURE

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Bronchial Hyper-responsiveness

Bronchial hyper-responsiveness (B.H.R.) may be defined as an exaggerated bronchoconstrictor response of the airway to a variety of stimuli which may be specific as house dust, mite allergens or non-specific as; exercise, inhalation of cold air or a variety of irritants and pharmacological agents *(Nadel and Pauwels, 1982)*.

These stimuli act through different specific mechanisms *(Pauwel et al., 1988)*; thus, categorization of airway responsiveness into specific and non-specific is confusing. The term specific was introduced to refer to the responsiveness induced by alleregens and chemical sensitisers which affect only those people hyper-responsive to them. Non-specific was used to describe the variety of non-allergic or non-sensitising stimuli which affected the majority of people with variable airflow limitation. However, the relative airway responsiveness to these different non-specific stimuli can differ between individuals. The term specific and non-specific should therefore be discontinued and substituted by the agent being used to measure responsiveness eg. methacholine airway responsiveness *(Dolovich et al., 1986)*.

Bronchial hyper-responsiveness may also be defined as a condition of the airways causing them to narrow excessively in response to a provoking stimulus *(Woolcock et al., 1989)*. Its acceptance as a component of asthma has led many workers to include it in their definitions of asthma some would go so far as to state that asthma can

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not be diagnosed in the absence of bronchial hyper-resonsiveness *(Adelroin et al., 1986)*.

It may also be defined as an exaggerated bronchoconstrictor reaction of smooth muscles and airway narrowing on exposure to a small quantity of non-allergic stimulus that does not provoke such a reaction in normal subjects *(Postma et al., 1989)*. On physiological basis bronchial hyper-responsiveness maybedefined as the tendency of airflow limitation (forced expiratory volume in the first second [FEV_1] and peak expiratory flow rate [PEFR] or specific airways resistance (SGaw) to increase in response to a lower dose of inhaled bronchoconstrictor stimuli (eg. histamine or methacholine) that needed to cause the same airflow limitation in a normal subject *(Flenly, 1990)*.

Relationship of Bronchial Responsiveness to Symptoms:

At any moment in time, only two thirds of clinically diagnosed asthmatic subjects have demonstrable hyper-responsiveness and one third of subjects demonstrating bronchial hyper-responsiveness are asymptomatic. This finding may be due to lack of correlation between the method of testing used in the laboratory and the process in nature that provoke attacks of airway narrowing *(Joanne et al., 1989)*.

There are also other psosibilities that deserve consideration for example, non-asthmatic members of families containing others with well defined asthma have a higher incidence of bronchial hyper-responsiveness when compared to the general population. A similar

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situation pertains for subjects with a past history of asthma *(Lang et al., 1987)*.

Bronchial hyper-responsiveness is also known to occur in association with diseases other than asthma eg. allergic rhinitis, chronic obstructive airway diseases, during and for four to six weeks after viral respiratory tract infection in non-asthmatic individuals *(Boushey et al., 1980)*, cystic fibrosis, exposure to inhaled sulphur dioxide or ozone, left ventricular failure and in cigarette smokers particularly over 50 years of age *(Flenly, 1990)*.

It is possible that asymptomatic subjects demonstrating bronchial hyper-responsiveness will subsequently develop asthma. Many other variables such as age, sex, and atopic status could also be responsible for the disparity between the presence of symptoms and the presence of bronchial hyper-responsiveness.

The degree of bronchial responsiveness correlates well with the severity of asthma symptoms and the medication required in asthmatic subjects *(Joanne et al., 1989)*.

Clinical Expression of Airway Hyper-reactivity:

Airway hyper-reactivity may manifest itself as episodes of cough, dyspnea, or wheezing after exposure to changes in temperature, especially from warm to a cold enviroment, exposure to chemical compounds, eg. sulphur dioxide, exhaust fumes, ozone, as well as fog, smoke, cooking smells, and exercise.

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The severity of the chest symptoms and the measured airflow obstruction depend both on the strength of the stimulus and the degree of airway hyper-reactivity; the stronger the stimulus, the lower the degree of airway hyper-reactivity necessary to induce bronchoconstriction ***(Postma et al., 1989)***.

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Importance of Airway Hyper-reactivity Testing in Clinical Practice

Bronchial hyper-responsiveness to histamine and methacholine is increased in virtually, if not all, subjects with current symptoms of asthma and CAO. The degree of increase has been found to be related to the current severity of symptoms and the number of previous hospital admissions *(Cockcroft et al., 1977)*. This does not implicate that one can interchange the degree of bronchial hyper-responsiveness with a symptom score on a questionaire since it has been shown that a questionaire is inadequate for discriminating between those with or without an increase of airway hyper-reactivity.

In clinical practice, this is also true; patients do not always present symptoms easily, they sometimes perceive airflow obstruction poorly or have lived for so long with variable airflow obstruction that they sense no airflow obstruction, whereas others interpret breathlessness as abnormal whenever it is present. Thus, some asthmatics seem much more aware of dyspnea than others despite similar degrees of airway obstruction *(Postma et al., 1989)*.

Burdon and his colleagues, (1982) studied the perception of breathlessness by using a standard histamine provocation test for quantification of airway hyper-reactivity and they found that, in general, breathlessness increased as FEV_1 decreased, however, some patients were unaware of dyspnea at a level of FEV_1 that would cause distress in others and if FEV_1 values were lower before the histamine challenge,

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