PHYSICAL GROWTH IN ASTHMATIC CHILDREN

Thesis

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Presented by

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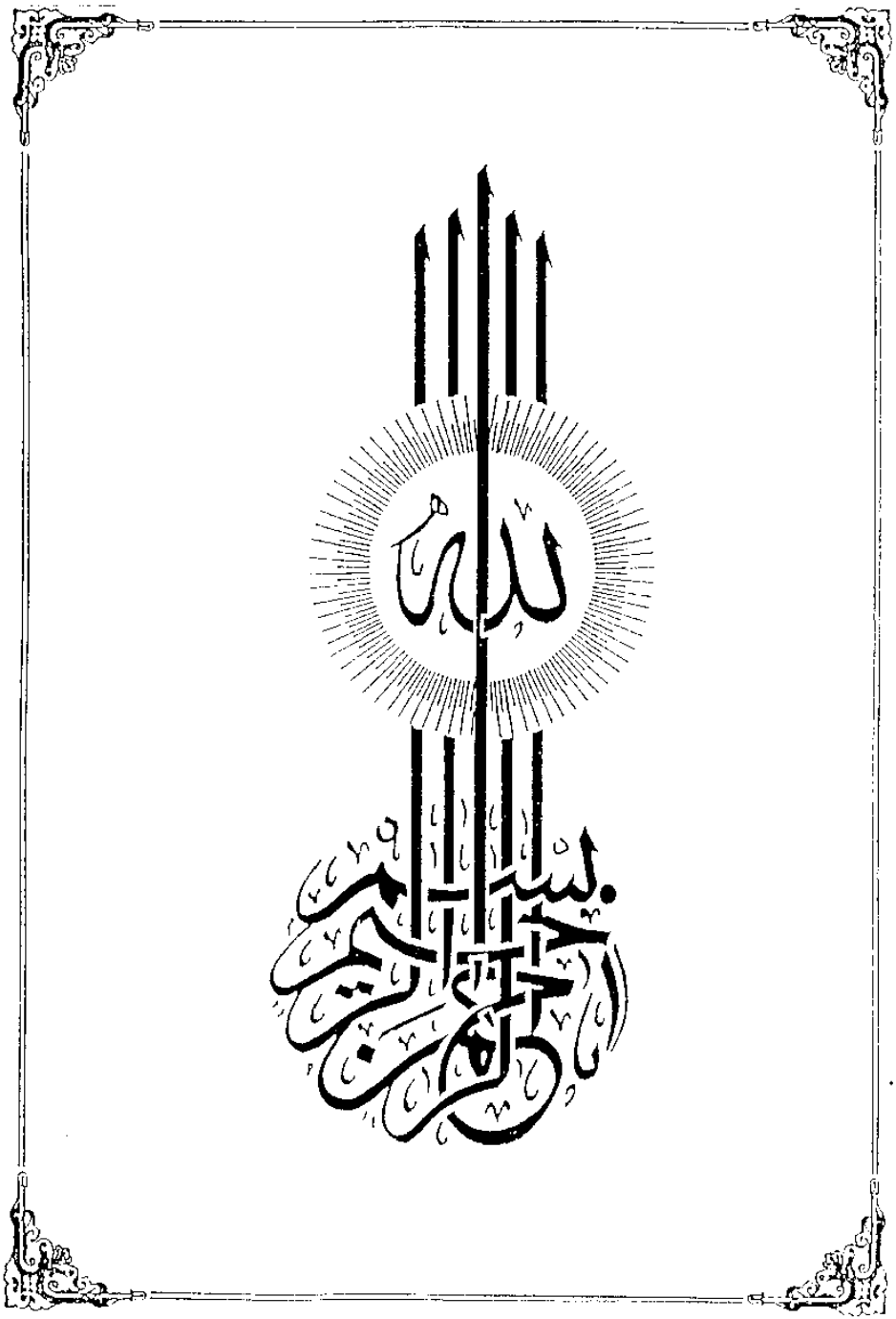

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INTRODUCTION AND AIM OF THE WORK

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Bronchial asthma is a major respiratory disease affecting approximatly 6 millions of children below the age of 12 years in the United States and has a significant morbidity and mortality. However, the true incidence of asthma is unknown and can be only estimated indirectly (Speizer,1968).

Asthma is responsible for a significant proportion of school days lost because of chronic illness.

Asthma can lead to severe psychosocial disturbances in the family. With proper treatment, however, much relief can be provided.

Underweight, understature and retardation of bone age have been reported in association with bronchial asthma (Von Metre et al.,1960 ; Falliers et al.,1961 ; Spock,1965).

Aim of the work :

This study aims to :

1) Assess the physical growth of children suffering from bronchial asthma.

2) Compare the physical growth of asthmatic children with that of non asthmatic ones of the same sex, age and socio-economic status.

BRONCHIAL ASTHMA

DEFINITION OF BRONCHIAL ASTHMA

Bronchial asthma is a complex disorder,which cannot be defined adequately in terms of a single pathophysiological mechanism, and there is no universal agreed definition of the word asthma (Proter & Birch,1971).

In 1962,the Committee of the American Thorathic Society defined asthma as a disease characterized by an increased responsiveness of the trachea and bronchi to various stimuli and manifsted by widespread narrowing of the airways that change in severity either spontaneously or as a result of treatment.

Scadding (1976) suggested that asthma is a disease characterized by wide variations ,over short periods of time, in resistance to flow intrapulmonary airways.

The basic problem in asthma is hyper-reactivity or "twitchiness" of the airways, causing the subject to develop bronchospasm in response to variety of stimuli (Burrows, 1979).

Bronchial asthma can be also defined as a recurrent generalized airway obstruction which ,at least in the early stages, is paroxysmal and reversible (Crofton & Douglas , 1981).

INCIDENCE OF BRONCHIAL ASTHMA

The true incidence of asthma is unknown and can only be estimated indirectly (Speizer, 1968).

The prevalence figures for asthma are very crude, and comparison between different surveys subjects to wide margin of error (Clark & Godfrey, 1977). The published figures suggest an asthma prevalence of 2.5% in primary achool children (Smith, 1961). In Egypt, the incidence of asthma among diseased children presenting to out-patient clinics of Children's Hospital, Cairo University, was found to be 2.2% (El Hefny, 1966).

Age of Onset:

Most serveys in Britain, North America and Australia have found that, in at least 30% of patients asthma began before the age of 10 years. In Scandinavia, India and Nigeria a childhood onset has been much less common (Clark & Godfrey, 1977).

Sex Incidence:

The great majority of surveys have found a male excess of asthma in childhood 1.5 : 1, and tendency to decrease as adolescence is approached (Blair, 1977). In adults there is little differences between sexes (Derrick, 1971).

In general, up to the age of 15 years, about 2.3% of boys and 1.2% of girls have asthma (Rhyne, 1974).

PATHOLOGY AND PATHOGENESIS OF ASTHMA

The main factors contributing to bronchial obstruction are the following :

(1) Bronchospasm :

bronchial muscle contraction is the most important component in the attack of the paroxysmal asthma (Crofton & Dougla, 1981). Contraction of the bronchial muscle in response to a specific allergen has been shown experimentally in human lungs resected from patients with allergic asthma (Schild et al., 1951).

(2) Swelling of the mucous membrane :

At autopsy, the bronchial epithelium of patients dying from status asthmaticus was found shed, thaugh the basement membrane was thickened with submucosal oedema and infiltration with eosinophils (Spencer, 1977).

(3) Plugging with viscous mucous :

Wanner and co-workers (1975) found an increase in the mucous glands and goblet cells, with plugging of the peripheral bronchi with viscid mucous in patients dying from status asthmaticus. This may be due to inability of the bronchial muscles to relax or replacement of ciliated cells by goblet cells. Less effective ciliary movement may also interfere with clearing mechanism,

(4) Invagination of posterior mucous membrane between the tips of semilunar cartilages of the intrathoracic trachea and the large bronchi on expiration, may play a rule in bronchial obstruction (Groen, 1976).

The pathogenesis of asthma is poorly understood. It may be due to: immunologic mechanisms, release of chemical mediators, pharmacological abnormalities or reflex pathways. All acting singly or in combination (Hinshaw, 1980).

I Immunologic Mechanisms :

Hypersensitivity reaction may be regarded as an exaggeration or distortion of a protective immunological process resulting in adverse manifestations in the individual (Kaltreider, 1976).

Gell & Coombs (1963) classified hypersensitivity reactions into 4 distinct types ; 2 of them mainly are concerned in asthma, namely type I and type III.

Type I hypersensitivity reaction :

This is an immediate or anaphylactic reaction, starting 10 to 20 minutes after exposure to the allergen in atopic response. It may be local reaction (atopy) as in skin e.g. dermatitis or in lung e.g. bronchial asthma , or it may be a generalised reaction leading to true anaphylaxis. This type of hypersensitivity reactions is mediated by immunoglobulin E (Ig E), which is synthesized in response

to exposure to a specific allergen, and gets attached to the surface of the mast cells. On subsequent exposure, the allergen combines with its specific IgE on the cell surface, causing the release of mediators from the granules of the sensitized mast cells (Hinshaw, 1980).

Stenius & co-workers (1971) reported a highly significant correlation between the presence and the amount of specific IgE against common allergens, such as grass pollens, and reaction they provoke in an inhalation test and clinical history of asthma. They stated that type I response can explain the majority of short lived attacks of asthma.

Johanson (1967) reported significantly raised serum levels of IgE in 63% of patients with allergic, as compared to 5% with non allergic asthma.

Sharaf El-Din (1982) found a significantly higher level of serum IgE in asthmatic than normal control children, with no significant difference between atopic and non atopic asthma.

Type III hypersensitivity reaction :

This is also called immune complex or arthus reaction. Immune complexes are aggregates of antigen and antibody with or without complement. The antibodies concerned are IgG and IgM. Antigens that evoke type III asthmatic reactions are numerous e.g. fungus Aspergillus fumigatus,

bacterial infections, drugs, wood dust, vapors and fumes (Colen et al.,1964).

Hargreave & Pepys (1972) suggested a role of type III reaction in late asthma when they observed a disproportionate fall in the forced expiratory volume in the first second (FEV_1), 4-6 hours after challenge, during the course of bronchial challenge studies on asthmatic patients.

II Chemical Mediators :

The physiologic consequences of exposing IgE-sensitized mast cells to antigen,against which the IgE molecule is directed, result from secretions of mast cell granules, from which derived chemical mediators of anaphylaxis (Metcalf et al.,1981). These chemical mediators may be preformed mediators, which are contained in the granule matrix (as histamine) and are released into the tissue fluid immediatly after reaction ; or they may be secondrily formed mediators, generated by interaction of primary mediators and nearby cells and tissues (e.g. prostaglandins).

Among the mast cell-derived mediators, those which are capable of causing bronchial smooth muscle contraction are :

1- Histamine :

Two cellular receptors for histamine have been identified, designated H_1 and H_2. Histamine-induced airway obstruction occures through stimulation of H_1

receptors on muscle fibers. In addition, there may be a vagally-mediated reflex parasympathetic action. Histamine also dilates the small vessels of pulmonary vascular tree, through an H_1 response, thus increasing the distance between endothelial cells of the venules, thereby increasing the potential for transudation of plasma for extravasation of leucocytes (Rosenthal et al., 1977).

2- **Slow-reacting substances of anaphylaxis (SRS-A) :**

SRS-A are though to be important mediators in man. The maxium effect on bronchial muscle is reached more slowely and is much prolonged than that of histamine.

SRS-A are composed of leukotreines (LT) C,D and E. These are pipridolipids derived from arachidonic acid, through lipoxygenase pathway. Studies on human bronchial muscle indicate that LTC and LTD are 1000 times more potent than histamine, and 500 times more potent than prostaglandin F_2 (Dahlen et al., 1980).

Weiss et al., (1982) stated that in normal persons LTC and LTD are the most potent bronchoconstrictor substances yet described, and that their prolonged duration of action is consistant with a possible role in mediation of IgE-mediated bronchoconstriction.

3- Prostaglandins (PGs) :

These are complex interacting group derived from products of arachidonic acid metabolism via a cycloxygenase-dependant pathway. The exact role of PGs in asthma is still unclear. Hyman (1978) reported that PGs form a complex interacting group, some members of which (PGE series) relax the bronchial muscle, while others (PGF series, specially $PGF_{2\alpha}$, PGD and Thromboxan A_2) are bronchoconstrictors.

Serum levels of PGF_2 and its metabolites have been shown to be higher in asthmatic attacks, and also an increase in PG metabolites have been found in urine (Green, 1974).

PGs are generated during the course of anaphylaxis. Through stimulation of H_1 receptors, histamine is responsible for about 50% of PG generated during anaphylaxis. On the other hand, bronchoconstriction selectively causes PGE generation, irrespective to the cause of the muscle contraction (Platshon & Kaliner, 1978).

III Pharmacological Abnormalities :

Szentivang (1968) suggested that the basic abnormality in asthma was impaired beta adrenergic responsiveness. This was termed the beta adrenergic theory. This theory was supported by Smith et al.(1980), who reported β_2 adrenergic hyporesponsiveness in atopic subjects if compared to control group.