THE RESPONSE OF NORMAL CHILDREN AND ASTHMATICS TO EXERCISE AND THE ROLE OF BRONCHODILATORS IN REVERSING EXERCISE-INDUCED ASTHMA

THESIS

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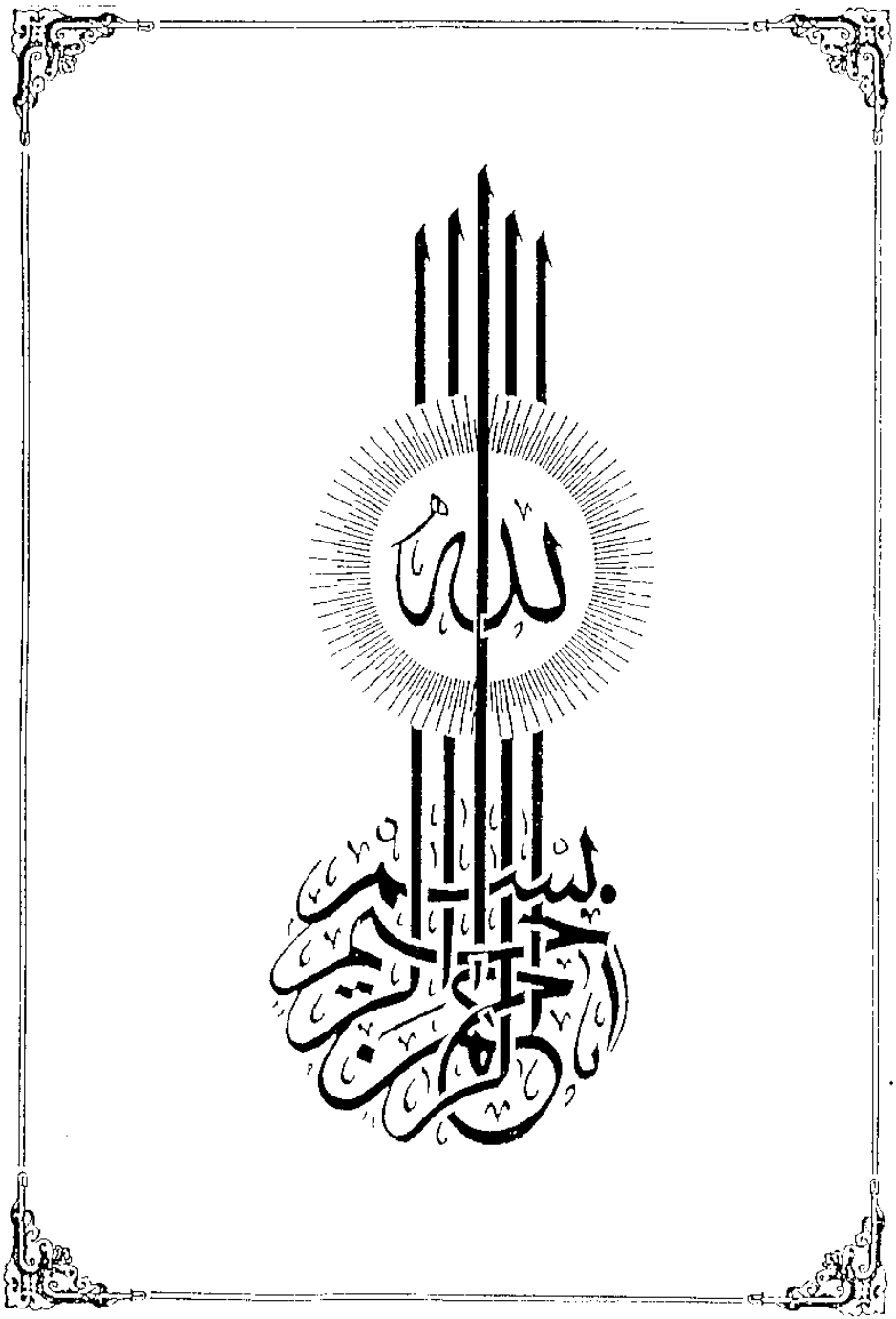

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INTRODUCTION

An asthmatic attack may be precipitated by many factors such as exposure to antigens, infections or chemical and physical irritants. Physical exercise frequently produces acute airway obstruction in both adults and children. The term exercise-induced asthma (EIA) is usually applied to this condition. Though EIA is common at all ages, it is particularly common in children. In many children a clear history of exercise-induced asthma is obtained and these children are frequently prohibited from taking part in physical activities. In others, exercise-induced bronchospasm becomes evident by doing pulmonary function test before and after exercise.

The acute episode of asthma induced by exercise is indistinguishable from that which develop from other causes, except that EIA is sudden in onset, short in duration, usually self-limited and always reversible (Cropp, 1975). A single exercise does not result in recurrent episodes of air-flow obstruction or status asthmaticus (McFadden, 1984).

Recognition, prevention and management of EIA is particularly important in children to allow them to participate in physical activities as their fellow friends and lead as normal a life as possible.

AIM OF THE WORK

This study aims to get an insight in the difference between the response of normal children and asthmatics to a standardised exercise test.

Also, the correlation between the severity of asthma as judged clinically (history and examination) and exercise-induced bronchospasm will be compared.

Finally, the effects of salbutamol and rimiterol hydrobromide will be compared in their role in reversing post-exercise bronchoconstriction in the asthmatic group of children.

Chapter II

A REVIEW OF THE LITERATURE

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DEFINITION OF BRONCHIAL ASTHMA

Asthma is defined by the American Thoracic Society as a disorder characterized by an increased responsiveness of the airway to various stimuli and resultant ventilatory obstruction. The latter results from bronchial smooth muscle contraction and is often accompanied by mucosal oedema and hypersecretion of mucous. These changes result in respiratory distress which is usually rapidly reversible either spontaneously or with treatment.

Another definition which is widely accepted is that of Scadding (1966) who defined asthma as a disease characterized by wide variation over short periods of time in resistance of airflow in the intrapulmonary airways.

VIRAL INFECTIONS AND OBSTRUCTIVE AIRWAY DISEASE

Viral infections of the respiratory tract are a major cause of episodes of wheezing, perhaps being the most common cause of acute wheezy illness in infancy and early childhood (Welliver, 1983). As many as 40% of acute wheezy episodes in young children are associated with recovery of viral pathogens in throat cultures (McIntosh et al, 1973). Henderson et al, (1979) isolated virus from 203 wheezy infant under two years of age. Of these isolates, 44% were Respiratory Syncytial Virus, 26% Parainfluenzavirus, 13% Adenovirus and 7% other viruses. These data agree

closely with other studies reviewed by McIntosh et al, (1973). It should be stressed that no evidence exists currently to support an aetiologic role of bacterial infection in asthma at any age (McIntosh et al, 1973, Horn et al, 1979, Hudgel et al, 1979). Of the virus implicated, Respiratory Syncytial Virus (RSV) is the commonest wheeze-associated respiratory illness. In early infancy, RSV is the commonest cause of bronchiolitis (Henderson et al, 1979).

An increase in bronchial reactivity after acute bronchiolitis and other lower respiratory tract infection has been shown in children. Whether this is fundamental and possibly related to atopic status or is acquired as a result of infection, perhaps by allergic mechanism is unclear (Godfrey, 1984). Rooney and Williams, (1971), Freeman and Todd, (1962), Konig et al, (1972) report that there is an increased incidence of personal and family allergy in bronchiolitis infants especially if they continue to wheeze.

On the other hand, Mok and Simpson, (1982), Sims et al, (1981), Pullen and Hey, (1982) find no such association between bronchiolitis and atopy.

It is postulated that RSV bronchiolitis causes a vigorous T-lymphocyte proliferation which leads to an excess of IgE production (Godfrey, 1984). The combination of the virus antigen with the cell bound IgE liberates excessive amounts of histamine and possibly other chemical mediators leading to

airway obstruction and wheezing (Godfrey, 1984). Clearly this vigorous immunological response could be due to an abnormality in the infant existing before acquiring the infection or it could be induced by the virus itself.

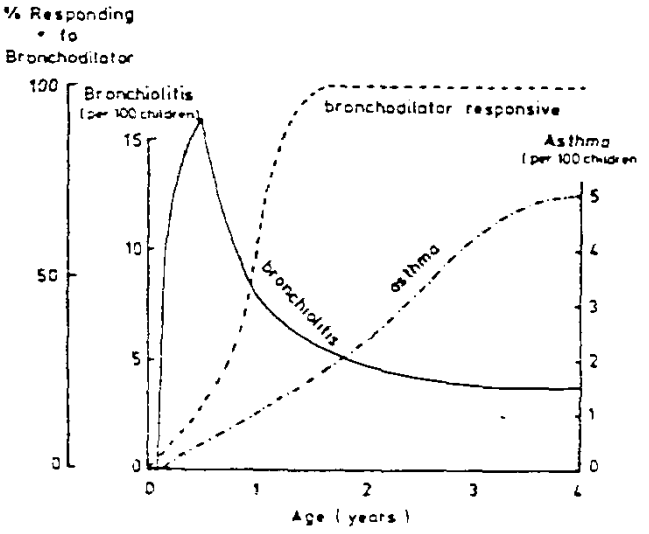
The origin of bronchial reactivity has been the subject of considerable debate. Studies of identical twins have shown that bronchial reactivity is not solely under genetic control, as normal or low level of reactivity has been found in identical twins of asthmatic subjects (Falliers et al, 1971). It has been suggested that bronchial reactivity requires both a genetic predisposition to the condition and an inciting event. This could explain why some children acquire bronchial reactivity after an acute respiratory infection while others do not. So, bronchiolitis and asthma are in fact two different entities which have a number of features in common and overlap in the age range in which they affect children.

Bronchiolitis can be regarded as a specific viral infection with a peak incidence in early infancy (6 months) which causes both cellular and humoral immunologic changes, and renders the infant susceptible to one or more further episodes of wheeze because of a modest percentage of induced bronchial hyperreactivity.

Conversely, children who have episodes of virus induced wheezing beyond 12 - 18 months of age with a history of personal or family allergy is

most likely to have asthma and may continue to have attacks for some years (Godfrey, 1984).

Between 6 - 12 months of age the classification of first time wheezes appears to be much less certainly due to the overlap of bronchiolitis and asthma at this age (Godfrey, 1984).



Schematic representation of the incidence of RSV bronchiolitis and asthma with respect to age based on published data (Denny et al, 1977). The proportion of infants responding to bronchodilators (Taussig et al, 1982) is also shown.

EPIDEMIOLOGY

Prevalence

It is estimated that 5 to 10% of children will at some time during childhood have signs and symptoms compatible with asthma (Ellis, 1983). For unknown reasons asthma is uncommon in New Zealand Highlanders, American Indians, Esquimos and West Africans.

In a study of clinic referral Speight, (1978) concluded that confusion over terminology and a long standing belief that the term "asthma" should be avoided when talking to parents might be responsible for much underdiagnosis and under-treatment. Only one-third of children experiencing greather than 12 episodes of wheeze were labelled as asthma. Two-thirds of children with history of wheeze did not receive bronchodilators and 55% of these children received antibiotics. This might be explained by a reluctancy of physicians to label their patients as asthmatics. This may be due to the longstanding paediatric tradition that the word asthma should be used only as a last resort when dealing with young children who wheeze. This was originally meant to avoid parental anxiety, but under-diagnosis and under-treatment of asthma are not justified whatever the reason. Prescribing expectorant and antibiotics will not help the asthmatics much.

96% of all children with asthma could be identified by the parents' reply to a single question "Has your child ever had attacks of wheeze?" (Speight, 1978). Diagnosis presents a problem only when doctors fail to ask specifically about wheeze, when parents volunteer less helpful symptoms such as cough or chestiness as children are often free of overt wheeze by the time they are seen. Laboratory test and special investigations are unnecessary for the diagnosis and management of most cases of asthma.

It can be emphasized that asthma is one of the commonest respiratory disorders of childhood.

Sex Distribution

Bronchial asthma is more common in males in early childhood (McNicol and Williams, (1973). According to Ellis, (1983), asthma is twice as common in boys prior to puberty. After puberty, the sex incidence is equal. This sex difference may be due to the fact that asthma in young girls is much milder and may pass unnoticed or not diagnosed as asthma. In those with infrequent episodes the distribution between boys and girls are equal (Phelan et al, 1982). In those children with frequent episodic asthma, 70% are males and 30% are females and in chronic asthma, the ratio of male to female is 4 : 1.

Age of Onset

Three to four per cent of children will have onset of wheeze prior to the age of 6 months, 60 to 65% between 6 months and 3 years and 30 to 35% between 3 years and 7 years (Phelan et al, 1982).

Morbidity

Asthma is one of the important causes of chronic illness in childhood. More school days are lost on account of asthma than any other chronic illness. Shira, (1973) reported that asthma is responsible for 22% of all days lost in school, 20% of total number of restricted activity days and 20% of days spent in the sick bed.

Effect on Growth

Infrequent episodes asthma has no effect on growth. Those who have frequent episodes of asthmatic attacks, the effect on growth is minor and in the past this was due to oral steroids. The availability of inhaled steroids now should not cause growth retardation. Those who have chronic asthma show growth retardation at 10 years and is maximal at 14 years (Martin et al, 1981). At 10 years, the retardation is mainly in height, but at 14 years it is both in height and weight.

Puberty is delayed in children with chronic asthma and this may be the major factor responsible for the retardation in height. By the age of 21 years, almost all subjects with asthma have achieved normal stature.

Mortality

Death in asthma has to be distinguished into the following groups:

-- death due to asthmatic attacks.