STUDIES ON THE IMMEDIATE AND DELAYED REVERSIBILITY OF AIRWAY OBSTRUCTION IN ASTHMATICS

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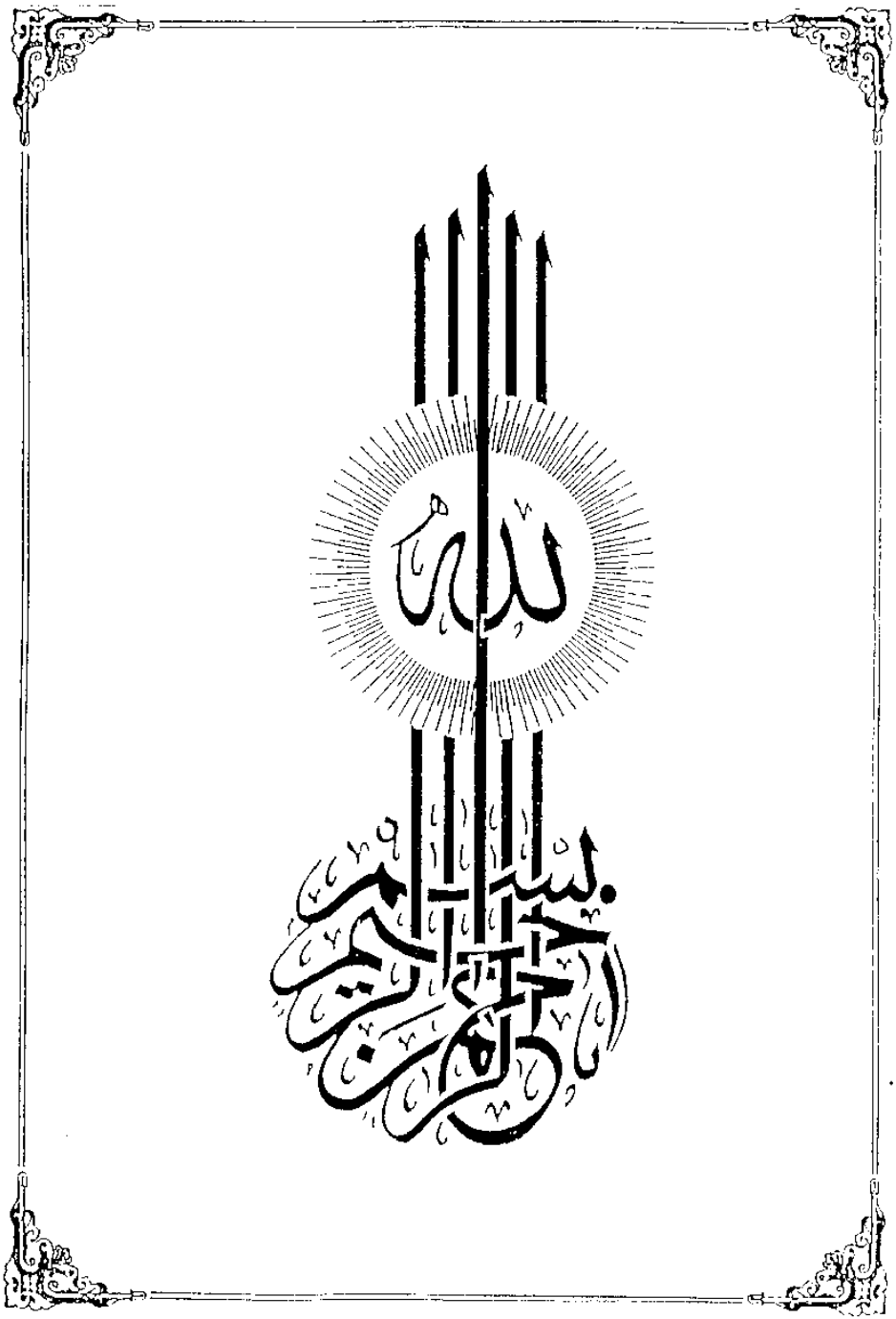

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INTRODUCTION AND AIM OF THE WORK

The usual test done in out patients asthmatic clinic to measure bronchial reversibility is salbutamol inhalation with spirometry before and after. However, clinical experience reveals that regular salbutamol inhalation for a week improves the bronchial obstruction, and additional beclomethazone inhalation can produce still more improvement.

The term overall total reversibility can be given to the improvement in the respiratory functions after one week salbutamol and beclomethazone inhalation.

The present study will quantitate short term and overall reversibility in cases of extrinsic and intrinsic asthma to allow a better understanding and quantition of obstructive bronchial diseases.

Glossary of Frequent used Terms

CAMP	cyclic adenosine mono phosphate
DSCG	Disodium cromoglycate
ECF-A	Eosinophilic chemotactic factor of anaphylaxis
FEV_1	Forced expired volume in the first second
FVC	Forced vital capacity
MBC	Maximum breathing capacity
MDI	Metered dose inhaler
NCF	Neutrophil chemotactic factor
PEF	Peak expiratory flow
$PFEV_1$	Predicted forced expired volume in first second
PVC	Predicted vital capacity
RV	Residual volume
SRS-A	Slow reacting substances of anaphylaxis
VC	Vital capacity

REVIEW OF LITERATURE

AIR WAYS HYPERREACTIVITY AND ITS MECHANISMS

Definitions of what constitute bronchial asthma still vary very greatly even today. In 1967 the united state National tuberculosis Association produced the definition : Asthma is a disease characterized by an increased responsiveness of the trachea and bronchi to various stimuli and made manifest by difficulty of breathing due to generalized narrowing of the airways. This narrowing is dynamic and changes in degree, either spontaneously or because of therapy. The basic defect appears to be an altered state of the host (USA National Tuberculosis Association, 1967). The altered state mentioned at the end of this definition refers to the hyperreactivity of the bronchial system, a character common to all patients with obstructive disease of the

aiways, and more specifically to the hyperreactivity of the bronchial system to stimuli. It is characterized by a recurrent bronchial spasm involving contraction of the smooth musculature of the airways, and acute mucosal edema and the immediate and excess secreation of a tenacious mucous.

Bronchial spasm of this type is evoked in hyperreactive patients by stimuli, among them we may distinguish between those of an exogenous origin (extrinsic) and others of an endogenous origin (intrinsic), the interplay of which determine the patency of the bronchial system. The most important of the many known ertrinsic factors are infection, airways contamination, inflammation and allergy, whereas our knowledge of the endogenous factors, which are bound up with

personality, remains rather fragmentary inspite of all the progress achieved in recent years. Special importance attaches in the connection to beta receptors tone, as defined by Ahlquist, which counteracts the bronchospastic property of the exogenous stimuli. (Ahlquist, 1948).

Allergy is the commonest mechanism of bronchial hyperreactivity via induction of formation of antibodies of immunoglobulin type E, which attaches to mast cells in bronchial wall, then a new exposure to the antigen will activates in these cells enzyme systems with release of histamine, slow reacting substances of anaphylaxis (SRS-A) and leukotriens. These will produce the acute airway obstruction. In the non atopic individuals immunoglobulin type

G is the causative antibody.

Ulmer et al., were able to show that the proteolytic enzymes released by bacteria or white cells sensitize the parasympathetic receptors of the airways producing an action similar to that exerted by mediators from Antigen - Antibody reaction (Ulmer, 1974).

Non specific physico-chemical stimuli like fumes, mechanical irritants and chemicals will produce reflex action, increasing bronchial tone from the sensitive receptors of the bronchial mucosa.

The way through which inflammation produce hyperreactivity may be an altered permeability of junctions between epithelial cells of

mucosa leading to reflex constriction of bronchioles via excitation of receptors normally protected by such junctions (Widdicombe, 1982).

Recently, a tryptic like enzyme, the tryptase has been shown to constitute at least- one third of the total protein in human lung mast cells. Thus we have a viable system in lumenal mast cells for breaking down these tight junctions and consequently increased bronchial reactivity (Empey, 1982). Current interest has centred on mediators of the cyclooxygenase and lipooxygenase pathways produced during inflammatory reactions (Kay et al., 1984, O'Byrne et al., 1984, Holgate et al., 1984).

Airway smooth muscle is under neurogenic

and myogenic control and thus bronchial hyperreactivity in asthma may be releated to an abnormality in one or other of these systems. Possible neurogenic mechanisms leading to hyperreactivity include an abnormality of vagal pathways, of alpha and beta adrenergic receptors in airway smooth muscles or of non adrenergic non-cholinergic nerves.

Because beta-agonists restore airway calibre towards normal in asthmatic patients, it was logical to suggest that a defect in beta - receptor function might underly bronchial hyperreactivity. Szentivanyi postulated that a generalized impairment in beta-adrenergic responsiveness was the underlying defect in asthma (Szentivanyi, 1968). This means that a higher dose of B- agonist was required to produce equivalent

bronchodilatation to normal subjects, but this may be due to impaired penetration of the inhaled drug with airflow obstruction and, more importantly, to functional antagonism, rather than a specific defect in b- receptor function (Barnes et al., 1983).

On the other hand, the good correlation between the increase in reactivity to stimuli acting through different mechanisms strongly suggests that there is an alteration in the intrinsic properties of the airway smooth muscle in asthma . These changes in the muscle could involve several mechanisms. An increase in the number of excitatory receptors on the smooth muscle whould lead to increased sensitivity to the agonist. Other mechanisms include an increase in contractility of individual muscle cells or an increase in