Bronchial Challenge Test in Bilharzial Patients

Thesis

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By

WAGDY HASSAN ABDEL MEGED EL ASRAG
M.B., B.Ch.

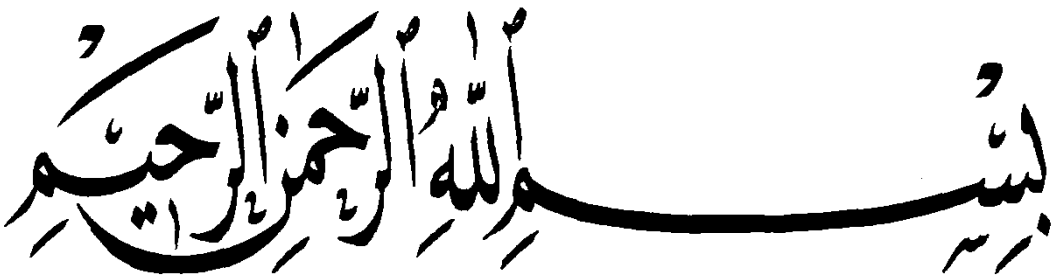
Supervisiors

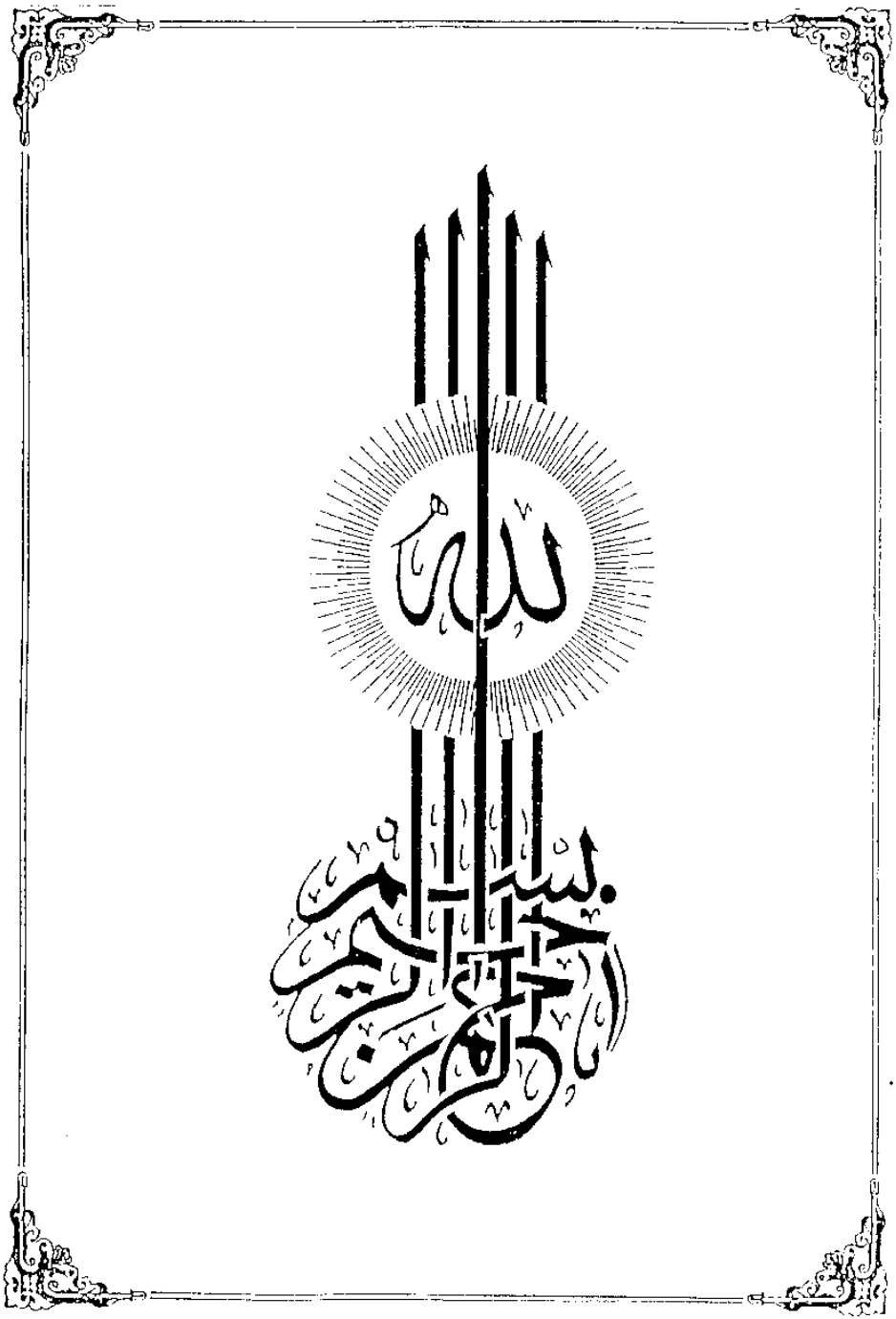
PROF. DR. ADEL GOMAA ALY
Professor of Chest Diseases & Chairman of
Chest Department, Ain Shams University

PROF. DR. HUSSEIN ALY HUSSEIN
Professor of Chest Diseases
Ain Shams University

DR. MANAL HOSNY
Lecturer of Chest Diseases
Ain Shams University

Faculty of Medicine
Ain Shams University
1994





بسم الله الرحمن الرحيم

(وفَوقَ كُلّ ذِى علمٍ عَليمٌ)

صدق اللّه العظيم

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Contents

Introduction

Schistosomiasis is the most important worm infection of man **(Mardsen & Hoskins, 1966)**. Pulmonary lesions are always secondary to urinary or intestinal infestation. They can be found at autopsy in one third of all cases of schistosomiasis **(Hinshaw & Murray, 1980)**.

Bellali (1885) was the first to detect schistosoma ova in the lung in post-mortem cases, while he was working in Alexandria. **Symmers (1905)** was the one who recognized worms in the lung blood vessels. **Saurez (1930)** was the first to describe a case of bronchial asthma he claimed to be schistosomial in origin. **Mainzer (1938)** described miliary infiltration in the lung due to schistosoma. He reported that not uncommonly, bilharzial patients present themselves with asthmatic or bronchitic symptoms.

In all the previously reported literature, there had been no mention of actual involvement of the bronchi by the ova. **Warraki (1961)** observed that the bronchial wall of schistosomial cases showed scanty blood supply which was attributed to the great involvement of arteriovenous shunts, this explains why bronchial system in these cases is susceptible to bronchial infection which is a common clinical association in cases of schistosomial hepato-splenomegaly.

Lung involvement in schistosomiasis is essentially an obliterative disorder of the pulmonary vessels which occurs as a result of multiple and repeated embolization of pulmonary arterioles by the ova of the parasite. Lung involvement after the ova get out of the blood vessels was described to be of two types: (1) parenchymatous lesions, which consist of granulomatous reaction in the form of tubercles which sometimes conglomerate to be seen pressing on the neighbouring respiratory bronchioles; (2) arteriolar lesions. There is intimal proliferation which will eventually result in obstruction of the pulmonary circulation and subsequent development of pulmonary hypertension **(Shaw & Ghareeb, 1938).**

Several studies described the relationship between bilharziasis and airway obstruction. Many authors find that there is obstructive pattern in term of decrease in FEV_1 in bilharzial patients, but none of them use bronchoconstrictive agent as a challenge to detect bronchial hyper-reactivity in these patients **(West, 1965).**

Bronchial hyper-responsiveness can be measured by a variety of stimuli which act through different mechanisms. The most common method of measuring airway responsiveness has been by inhalation of histamine or metacholine, or by exercise tests. Other stimuli include hyperventilation in cold dry air, hyper-ionic saline, leukotrienes LTD_4 and LTC_4, prostaglandin $F_{2\alpha}$ and $D_{2\alpha}$, neurokinin A, adenosine monophosphate, propranolol, and bradykinin **(Hargreave et al., 1989).**

Aim of the Work

The aim of this work is to study the relation between bilharzial infestation and bronchial hyper-responsiveness by using metacholine inhalation bronchial challenge test.

Review of Literature

Chapter I. Bronchial Hyper-Reactivity

Definition

Bronchial hyper-responsiveness may be defined as an exaggerated bronchoconstrictor response of the airways 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 & Pauwels, 1982)**.

It may also be defined as an exaggerated bronchoconstrictor reaction of smooth muscles of airways narrowing on exposure to a small quantity of non-allergenic stimulus that does not provoke such a reaction in normal subjects **(Postana, 1989)**.

Its acceptance as a component of asthma had led many workers to include it in their definitions of asthma. Some would go so far as to state that asthma cannot be diagnosed in the absence of bronchial hyper-responsiveness **(Adelrion et al., 1986)**.

One of the characteristic features of asthma and a feature that occurs in some patients with chronic bronchitis and allergic rhinitis is the extreme sensitivity of the airway to physical, chemical and pharmacological stimuli. These patients develop a greater degree of

bronchoconstriction in response to a wide variety of stimuli than do healthy subjects.

Mechanism of Bronchial Hyper-Responsiveness

The mechanism underlying the development of bronchial hyper-responsiveness all remain obscure. Several mechanisms can be involved, including a decrease in baseline caliber, an increased responsiveness of the smooth muscle itself, an abnormality in the autonomic nervous control of smooth muscle, an increase in the accessibility of stimuli to the target cells, or changes in cell permeability to Ca^{++} **(Sheppard, 1988)**.

1. Decreased Baseline Airway Caliber

The caliber of the airway in the baseline state can influence the subsequent response to agents that induce bronchoconstriction. Most in vivo tests of airway narrowing depend directly or indirectly on changes in airflow resistance because the resistance is inversely proportional to the fourth power of the radius when the flow in the airways is laminar. Any decrease in the radius of a narrow airway causes a greater change in airway resistance than does the same decrease in the radius of a dilated airway **(Boushey et al., 1980)**.

Although changes in the baseline airway caliber may be important under some conditions, they do not explain the differences in bronchial reactivity in a variety of circumstances. Several studies have shown large differences in bronchial reactivity among different subjects when baseline values of airway resistance were similar **(Hahn et al., 1979)**.

2. Alteration in Smooth Muscle

Increase in the amount of airway smooth muscles and airway thickness probably contribute to the increased airway responsiveness of severely asthmatic subjects. However, they cannot be the cause of hyper-reactivity that occurs transiently in normal subjects during viral infections **(Empey et al., 1976)** or after exposure to oxidizing polluants **(Golden et al., 1978)** because the smooth muscle is unlikely to change in a short period of time.

3. Disorders of Autonomic Regulation

Airway hyper-reactivity could be due to increased para-sympathetic or alpha adrenergic activity or to decreased beta adrenergic or noradrenergic inhibitory system activity.

A. Parasympathetic Nervous System

The parasympathetic efferent nerve supply to the airways is via the vagal nerves, the preganglionic vagal fibers travel from CNS to parasympathetic ganglion fibers from these ganglia extend to airway smooth muscle. Electrical stimulation of the peripheral ends of the cut vagal nerves causes bronchoconstriction **(Boushey et al., 1980)**.

The fact that this response is potentiated by acetyl choline esterase inhibitors and is blocked by atropine provides evidence that the vagal nerves cause bronchoconstriction by release of acetyl choline at the post ganglionic endings of the muscles **(Olsen et al., 1965)**.

The distribution of constriction mediated via the vagus has been shown to be maximal in the small bronchi and absent in the small bronchioles and alveolar ducts. A mild degree of resting tone normally exists in airway smooth muscle in animals. This tone is mediated by vagal efferent activity and is blocked by atropine **(Nadel et al., 1971)**.

In patients with asthma, atropine is reported to be equivalent in potency of bronchodilatation to β-adrenergic agonists, suggesting that the increased airway smooth muscle tone in this disease may be due to increased vagal nervous activity. The origin of normal vagal tone and the increases in tone in disease could be due to reflex bronchoconstriction initiated by stimulation of sensory pathways due

to outflow directly from CNS, or due to effects on vagal efferent pathways themselves. Multiple receptors have been shown to affect bronchomotor tone including those in the nose, larynx and lungs, as well as chemoreceptors and baroreceptors located elsewhere **(Cropp, 1975)**.

One of the most interesting bronchoconstrictor reflexes is initiated by stimulation of receptors in the airways themselves, the receptors appear to lie immediately beneath tight junction between epithelial cells in the airways. These endings probably represent the irritant receptors that are stimulated by inhalation of dust chemical irritants and drugs, such as histamine and metacholine **(Widdicombe, 1977)**.

Definitive proof of reflex bronchoconstriction is derived from experiments that stimulated sensory endings of smooth muscle, thus mechanical irritation of the larynx and delivery of sulphur dioxide only to upper airways, caused bronchoconstriction of the lower airways. Histamine injected into the bronchial arteries resulted in constriction of a by-passed tracheal segments not perfused by the bronchial arteries. All these effects were abolished by cutting the sensory input from the lungs. Neural output from the CNS in the absence of the sensory input from the lungs could also be responsible for vagal efferent activity. The fact that this bronchoconstriction is abolished by cholinergic antagonists suggests that the parasympathetic nervous system plays a role. In asthma, the role of emotion on the airways is assumed to be expressed through the parasympathetic nervous system. A significant number of asthmatic

subjects respond to psychological stimuli with bronchoconstriction **(Horton et al., 1978)**.

B. Sympathetic Nervous System

The sympathetic nerve supply to lungs originates from upper thoracic pre-ganglionic fibers that end in the extra pulmonary satellite ganglia. Post-ganglionic fibers can be visualized in the walls of the airway and surrounding blood vessels by fluorescent histochemical test for catecholamine. Adrenergic fibers to the smooth muscles have not yet been demonstrated in humans **(Richardson & Beland, 1976)**.

Although there is good evidence for vagal bronchoconstriction activity in animals and in humans, the role of sympathetic nerves in the regulation of resting smooth muscle tone is less clear. In dogs, cutting the thoracic sympathetic nerves results in a small increase in airflow resistance **(Green & Widdicombo, 1966)**.

These studies suggest that a small degree of sympathetic dilator tone normally exists in the airways. The usual response to electrical stimulation of the thoracic sympathetic nerves is bronchodilatation, and this effect is abolished by β-adrenergic antagonists. The effect of sympathetic nerves stimulation depends on the prior existing level of vagal smooth muscle tone, thus in dogs, when the vagi were cut, stimulation of the thoracic sympathetic nerves had no effect on airway dimension, presumably because airway smooth muscle tone