THE ENDOCRINE PROFILE OF BRONCHIAL ASTHMA

Review of the literature and study of thyroid function

THESIS

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by

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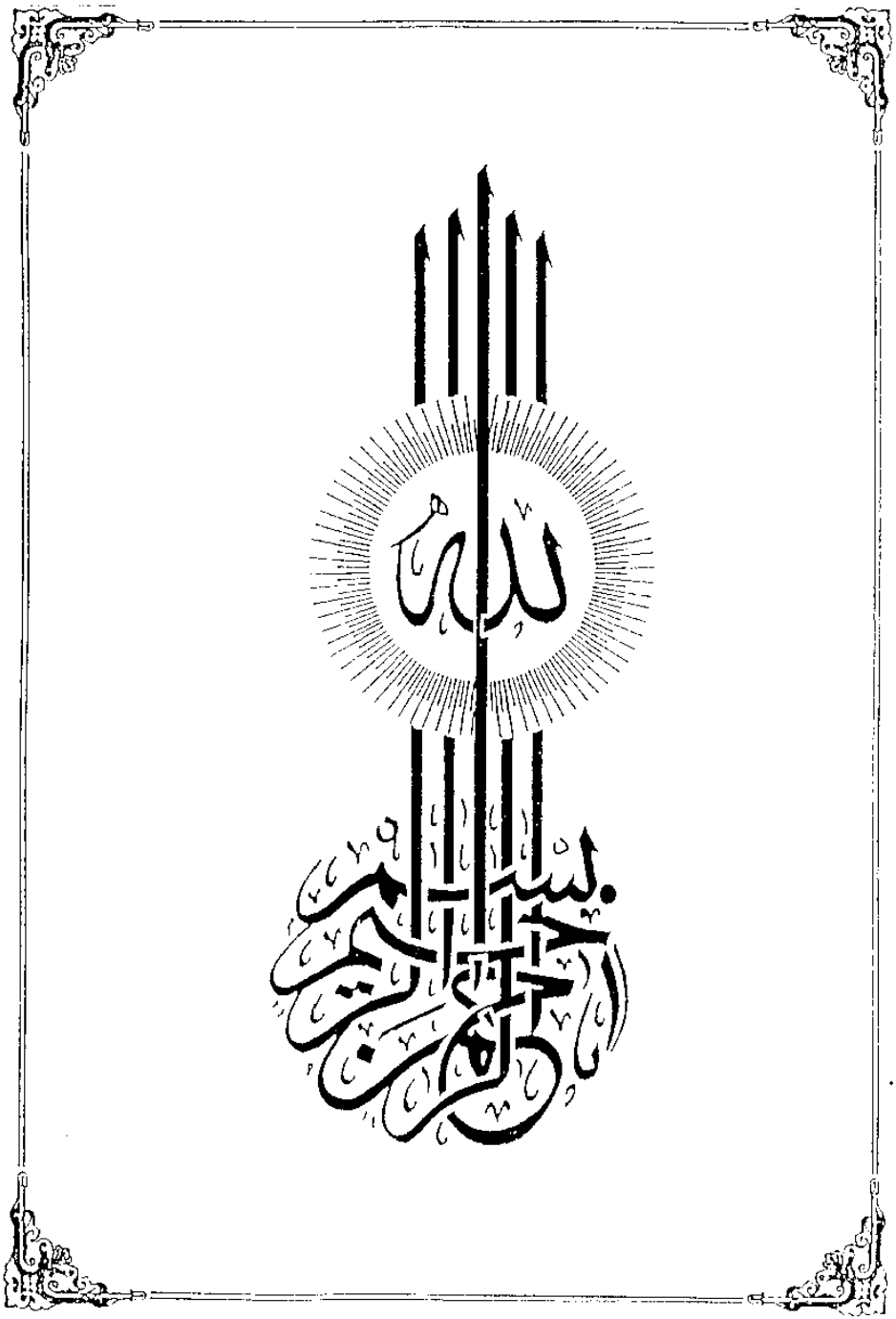

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INTRODUCTION AND AIM OF THE WORK

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Asthma is a common condition and, although considered a benign disorder by some, is responsible for a significant number of deaths annually.

It is also a disease responsible for a great many days of absence from school or work and is an important disease from the socioeconomic point of view.

Continual research aims at better understanding of the pathogenesis of the disease hoping to reach to better lines of treatment.

Here we aim to explore the endocine profile of the disease.

This thesis deals with the thyroid gland function with bronchial asthma.

The introduction of radioimmune assays, has facilitated the assessment of the thyroid functions in a more precise and accurate way.

With this idea in mind our work will be conducted to investigate the thyroid function by the estimation of : Serum thyroxine (T4) and triiodothyronine (T3) levels during asthmatic attacks.

REVIEW OF LITERATURE

DEFINITION AND CLASSIFICATION

Bronchial asthma is a varible, intermittant - reversible obstructive pulmonary syndrome that includes many bronchospastic airway disorders. It is characterized by recurrent periodic episodes of paroxysmal wheezing - frequently associated with dyspnea and cough due to - obstruction of expiratosy airflow, it may occur seasonally or Perennially. The periods between attacks are symptom free, (Criep 1976) or bronchial asthma could be difined as a tendency to transient attacks of dyspnea by bronchial obstruction, it may occur at any time of day or the night but most usually in the evening during the night or in the early morning. The obstruction may be brought about by spasm of the bronchial muscle or by oedema of the mucosa or by mucus secreted into the bronchial lumen or by any combination of these three factors . (Herx heimer, 1975)

It is quite clear, there fore that the definition of the asthma means intermittent quickly developing and spontaneously resolving bronchial obstruction always - consisting of bronchial muscular spasm, but sometimes also oedema and hypersecretion occur .

. Classification of asthma

A- Extrinsic asthma : (Asthma triggered by enviromental substance)

1- Extrinsic immediate atopic asthma: Which explained primarily by the type 1 immunopathologic reaction. Although an underlying defect in autonomic regulation also may be present, yet it may be present in one way or another in all forms of asthma. Aeroallergens that may provoke this type of asthma include tree weed, grass, Pollens, animal epithelials, dust and mold particles. (Lockey and Bukantz, 1978)

2- Extrinsic late non-atopic allergic asthma

Asthma begins at least one hour following exposure to airborn allergens This may be secondary to a modified type 1 reaction or to an immunoglobilin other than IgE , i.e., an IgG homocytotropic antibody. Some individuals with hyper sensitivity pneunonitis wheeze follozing antigenic exposure. This type of asthma may be secondary to type lll and/or type IV immunopathologic reaction (Ibid.)

3- Extrinsic irritant and pharmacolgic asthma:

An immunologic basis for these diseases has not established. Most asthmatics are exacerbated by chemical exposure. Some chemicals appear to cause asthma by their direct irritant effct on bronchial

mucosa and others by unexplained pharmacologic mechanism. The mechanism for this form of extrinsic asthma, however, remains unkown. (Ibid)

B- Intrinsic asthma:

Also called non allergic asthma or infective asthma (Herxhemier, 1975)

sub groups of intrinsic asthma are:

(1) Intrinsic aspirin - intolerant asthma

(2) Intrinsic infectious asthma:

Common in children. These asthmatics are susceptible to recurrent viral upper respiratory infections which cause asthma. Bacterial infections rarely cause asthmatic exacerbations. Patients are ususally well between infections and become less symptomatic with age . This clinical profile of asthma also occurs in adlut (Lockey and Bukantz, 1978)

(3) Intrinsic exercise - induced asthma

It is primairly seen in children who wheeze only after vigorous exercise. Exercise induced bronchospasm is commonly seen in association with many forms of asthma. (Crop 1978)

(4) Intrinsic asthmatic bronchitis:

This is a combination of asthma and chronic bronchitis The patients may or may not have been smokers, however both asthma and bronchitis play an important role in the clinical presentation . (Lockey and Bukantz, 1978) Although this division in useful, it cannot be strictly maintained because there are cases of allergic asthma which at times become infected and thus must be regarded as mixed allergic and infective asthma (Herx heimer, 1975).

PATHOGENESIS OF BRONCHIAL ASTHMA

Bronchial asthma is a heterogenous disorder - characterised by a revesible airway obstruction which could result mainly from contraction of airway smooth muscle or true broncho spasm, other factor which would contribute to bronchial obstruction are those relalated to mucus hypersecretion, mucosal oedema and plugging of the bronchi viscid mucus.

1- Abnormal autonomic mechanisms:

Bronchial hyperreactivity:

Normal subjects may inhale a variety of irritants such as smoke, dusts in certain concentrations, aerosols of pharmacological agents such as histamine, carbachol or methacholine with little or no change in airway resistance by contrast subjects exist in whom inhalation of these agents provoke bronchoconstriction. i.e they exhibit bronchial hyperreactivity. (Howell, 1976)

The mechanism of hyperreactivity is uncertain but the rapidly of isoprenaline to reverse repidly the changes, is strongly suggests that constriction of bronchial muscle is the dominant reaction whether it is due to direct effect of the agent upon the

tissues or due to a reflex response mediated by the vagi is also uncertain and there is evidence that either or both mechanism may exist. (Ibid)

Gold (1973) reported that in dogs sensitised to intestinal parasites, the relevant antigen instilled - intrabronchially into one lung resulted in generalised bilateral bronchoconstriction. Vagotomy prevented this development. On the other hand, direct hyperreactivity has been shown on isolated tracheal rings from patients with chronic airway obstruction in which vagal reflex could not possibly have been involved.

Benson (1975) added evidence that at least a part of bronchial hyperreactivity is a consequence of - bronchoconstriction and of increased bronchomotor tone.

Infections and other irritants may stimulate the hyperreactivity bronchi directly or reflexly, emotional reactions act by increasing autonomic vagal discharge and the same mechanism may account for nocturnal attacks of asthma (Howell, 1971)

A- Cholinergic supersensitivity and parasympathetic cholinergic reflex:

For more than 30 years aerosols of histamine and cholinergic agonists have been known to cause vigorous bronchoconstriction in patients with asthma.

Normal persons respond with a slight bronchoconstriction detectable with sensitive techniques, but the response of patients with asthma is 100 to 1,000 fold greater (Reed, 1974).

In normal subject, stimulation of sensory receptors in the submucosa of the larynx or central airways causes coughing and bronchoconstriction. Stimulation of similar sensory receptors in the more peripheral airways causes rapid breathing and bronchoconstriction Thus inhalation of sulfur dioxide, inert dust, or mechanical stimulation of the airway mucosa aresults in bronchoconstriction that can be prevented in animals by cutting the vagi, and in human by atropine.(Ibid)

Asthmatic subjects develop bronchoconstriction from concentrations of agents too low to evoke a response in normal subjects (Ibid)

This excessive response can be attenuated by prior administration of atropine (Simonsson et al, 1967).

Histamine stimulates the irritant receptors of the airway (Sellick et al, 1971). Although histamine is able to constrict the smooth muscle of the airway directly, most of the bronchoconstriction effect of this drug in normal dogs is exerted via the vagal reflex (Reed, 1974)

In dogs Gold & his colleagues have illustrated the importance of the vagus in experimental asthma in dogs. They have showen that blocked of either the afferent or the efferent pathways of the vagus greatly reduces antigen induced bronchoconstriction Challange by antigen aerosol delivered to only one lung caused bronchoconstriction in both lungs. Unilateral cooling to a temperature that blocked afferent but not efferent fibres of the vagus of the challenged lung prevented the reaction in both lungs as effectively as transection of both vagi (Thurlbeck and Bennington, 1976).

Thus reflex vagal bronchoconstriction appears to play a critical role in expermintal asthma in dogs.