THE ROLE OF IMMUNE COMPLEXES IN THE AETIOLOGY OF INTRINSIC ASTHMA

Thesis

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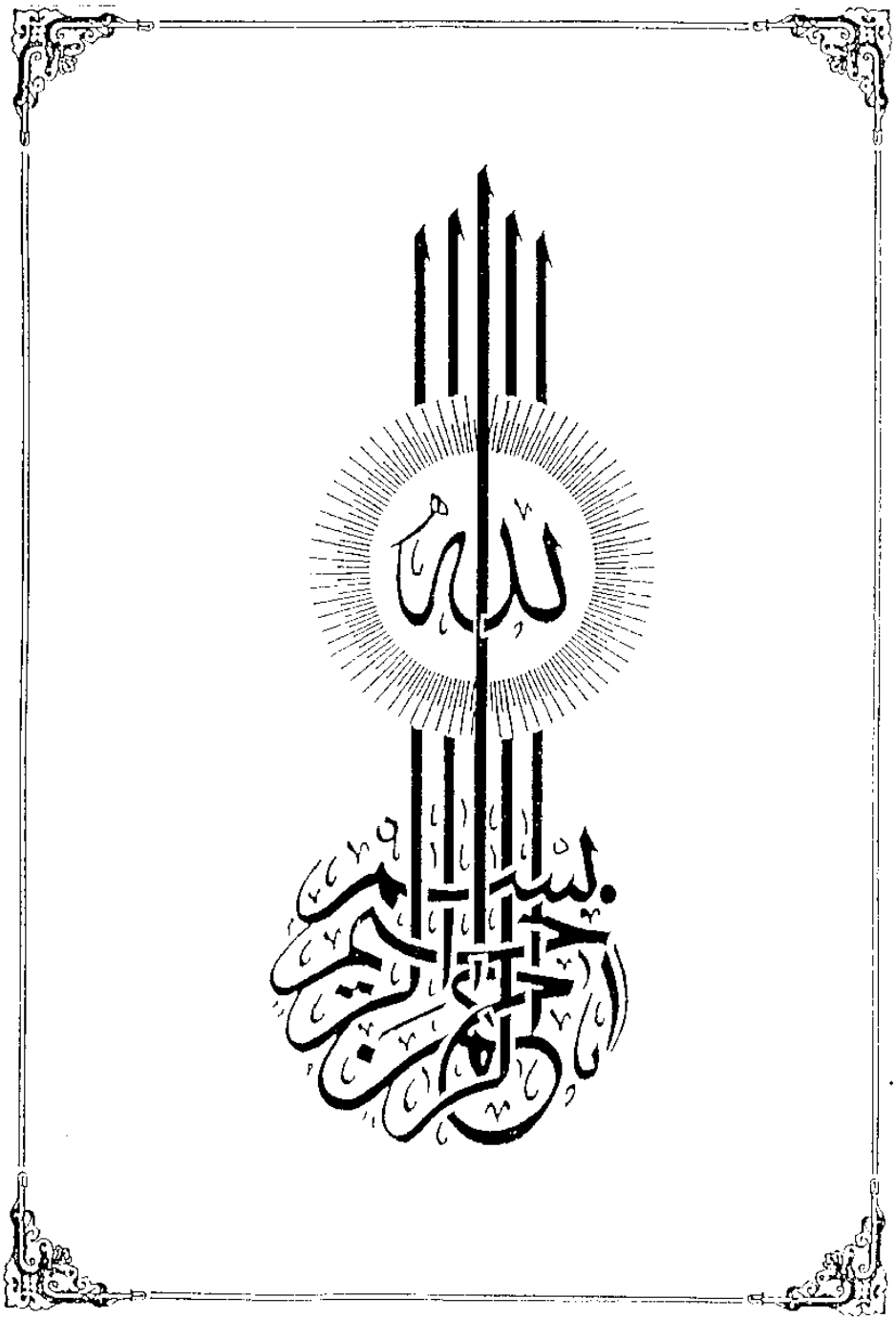
This thesis is dedecated

to

My mother, my wife, my children

Mira and Mina

and to the memory of my father.



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CONTENTS

AIM
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The aim of the present study is detecting immune complexes in the sera of patients with chronic intrinsic asthma and measuring their levels . The results will be compared with sera of normal individuals, to know the role of immune complexes in the aetiology of intrinsic asthma.

INTRODUCTION

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Bronchial asthma is a major cause of respiratory difficulty. It ranges in sevirity from mild forms to life-threatening and incapacitating tragedies (Aas K., 1981).

There is no classification of asthma that satisfactorily incorporates all situations in which reversible airways disease occurs. It has become popular to recognize asthma clinically as extrinsic and intrinsic asthma (Costello,J.F. 1980) . The pathogenesis of intractable chronic asthma with negative skin test is not yet settled. The term intrinsic asthma given to those patients indicates this fact.

It has become certain that type III reaction plays a considerable role in asthma due to various allergens, e.g. Aspergillus Fumingatus, proteolytic enzymes extracted from B. subtilis, avian protein antigen (Pepys et al 1969), and ragweed pollen allergen (Robertson, G., et al , 1974). Precipitating IgG antibodies against these allergens have been identified in the sera of those patients.

The probable implication of the complement system in " late onset " or " non-atopic " asthma was emphasized in a study of 31 bronchial biopsy specimens from patients with asthma.The presence of IgA. IgG and IgM was constantly associated with C_3 (Rose, B. et al 1978).

Cunningham-Rundles et al 1978 , suggested that foods have

to be considered potential sources of antigen in patients with immune complex diseases of unknown aetiology.

Pepys, suggested that asthmatic patients, previously classified as intrinsic or cryptogenic may be re-classified as extrinsic. This is occuring , for example, where extrinsic causes acting in non-atopic fashion are identified. (Pepys, J., 1981).

LITERATURE REVIEW

HISTORICAL

The word asthma is drived from a Greek word and signifies panting. Originally it was used as a general term to discribe the symptoms of virtually all respiratory illness and as a synonym for breathlessness.

Although the Hippocratic writings contain a few references to asthma, the first detailed discussions did not occur until the second century of the Christian era, when Aretaeus the Cappadocian and Galen both wrote about it. Areteaus recognized that the disorder was chronic with an episodic nature, that it affected adults and children, and that it occured in both sexes. He also provided a description of an acute paroxysm, but he confused asthma with other causes of breathlessness.

Galen also did not differentiate asthma from similar diseases and attributed most, if not all, forms of respiratory embarrassment to an intermittent impediment to respiration that was secondary to excessive and thick secretions that dripped into the lung from the brain, through the nasopharynx. Galen's ideas on descending brain secretions gave rise to treating dyspnea by purging the nostrils so as to relieve the brain and to clear the air passages of the lung. This practice continued until the seventeenth century.

The next two works of significance were those of Paulus

Aegineta and Moses Maimonides. Paulus, who lived in the seventh century, is important historically because he had extensive knowledge of Greek, Roman and Arabian medical practices, which he summarized. His description of severe respiratory distress was quite detailed clinically, but his views on pathogenesis and therapy differ little from Galen's. In the twelfth century Maimonides wrote that " the soup of fat hens is an effective remedy in asthma" he laid a precedent so powerful that it has endured in the pharmocopoeia of grandmothers until the present time.

In 1552 Girolamo Cardano, A milanese physician, astonished his colleagues who were attending the Archbishop Hamilton of St. Andrews when he relieved the Archbishop's asthma by removing his feather bed and feather pillows.

In 1662 Van Helmont associated the symptoms of asthma with the change in seasons and noted that acute exacerbations could be brought about by inhalants such as dust or ingestion of certain foods. Each of these observations lay dormant for several more centuries before their significance was recognized.

Near the end of the seventeenth century, Galenic concepts of the pathogenesis had been virtually abandoned. Thomas Willis believed that asthma was caused by humoral factors, and he reasoned that the asthma was due to

alteration in the muscles of the "bronchia", in the nerve fibers, or within the brain because of nervous input. The first book devoted entirely to asthma was written by Sir John Floyer in 1698. He believed in Willis' humoral concepts, he also felt that mechanical factors were important.

Floyer classified asthma into " continued or periodical" types and recognized that intrapulmonic infections, tracheal obstruction, thoracic deformities, and "coagulation of blood in the vessles" could all be associated with "continued asthma". The "true periodic flatulent asthma" however, was associated with emotions, laughter, hysterical fits and often followed a "catarrh". He also described exercise induced asthma. In addition, he made the first recorded observation of pulsus paradoxus during an acute attack. Despite his achievements, Floyer did not distinguish asthma from chronic bronchitis.

In 1761 Morgagni described the bronchial concretions that are typical of death from status asthmaticus, he also described asthma in a hemp handler and in man who made feather beds. In 1769 John Millar gave weight to the concepts of Floyer regarding "periodic asthma" by describing the natural history of the disease in children. In doing so, he allowed for better separation of asthma from other diseases with which it was confused in adult life.

In 1802, treatment with atropine began in England, and the observation was made that the postmortem findings in an asthmatic lung showed minimal structural changes other than hyperinflation. In 1803 Reisseissen demonstated that circular muscle fibers surrounded the airways and that if these fibers constricted, the airway could narrow, thereby providing structure to function insight concerning the spasmodic nature of this disease.

In 1819 Laennec, using the stethoscope, identified the characteristic sounds of asthma. In the same year, coincident attacks of asthma and conjuctivitis that recurred each summer were described, anticipating current concepts of variations in target organs in atopic disease. The development and use of the microscope led to related observations of eosinophils in the sputum of asthmatic patients.

In 1830 John Eberle stated "It is highly probable that asthma consists essentially in a peculiar irritation of the pneumo-gastric nerves (vagus), in consequence of which the smaller bronchial tubes and air-cells are thrown into a state of spasmodic constriction". but he dismissed the work of John Millar on childhood asthma .

By the latter half of the nineteenth century, most authorities could separate asthma from other conditions