# EOSINOPHILIA-MYALGIA SYNDROME

THESIS
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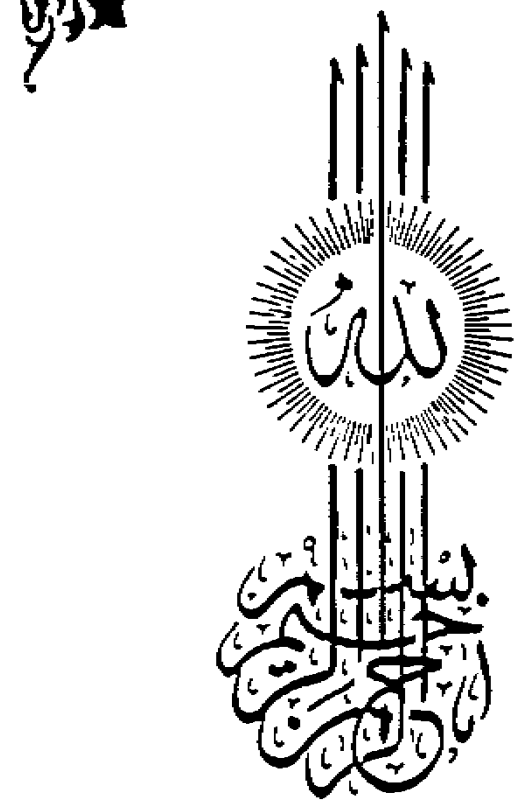
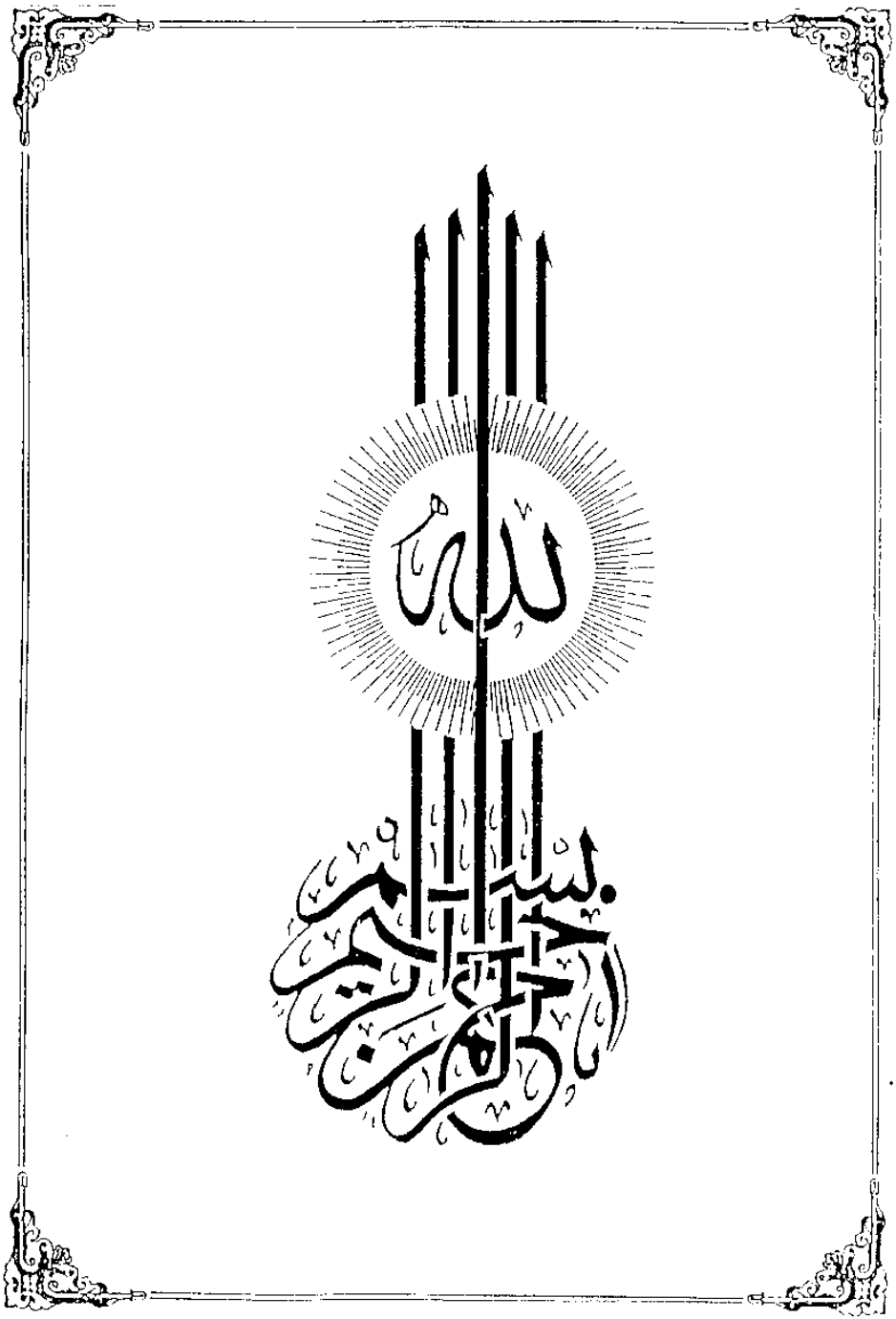



وَمَا أُوتِيتُم مِّنَ الْعِلْمِ إِلَّا قَلِيلًا

صدق الله العظيم

"الإسراء ٨٥"



" TO MY PARENTS

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# " ACKNOWLEDGMENT "

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It is of a great honour to express my deep gratitude and appreciation to **Prof. Dr. Nagwa Mohamad Youssef,** professor of Dermatology and Venereology, Faculty of Medicine, Ain Shams University for her kind guidance, continuous encouragement and great help.

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# " INTRODUCTION "

# INTRODUCTION

## EOSINOPHILIA - MYALGIA SYNDROME

The eosinophilia-myalgia syndrome (EMS) is a recently recognized clinical entity that was first described in the United States during the summer of 1989 **( Hertzman et al., 1990 ) .**

The syndrome was proved to be related in some way to ingestion of L-tryptophan, an essential amino acid marketed as a nutritional supplement and widely used as a therapeutic agent without adequate medical supervision **( Varga et al., 1993 ).**

L-tryptophan is the scarcest of the amino acids , and vertebrates depend on exogenous sources of this essential amino acid **( Silver, 1991 ).** Particularly high amounts of L-tryptophan are found in meat, poultry, fish, milk, and cheese **( Blauvelt and Falanga, 1991 ).** The average daily American diet contains approximately 1gram of L-tryptophan which is more than adequate for the nutritional needs of most individuals **( Silver, 1991 ).**

L- tryptophan reduces sleep latency in humans and has been considered to be a natural hypnotic. Because serotonin plays an important role in the mediation of sleep, it has been assumed that the effects of L-tryptophan result from increased availability of serotonin in the brain **( Young and Teff, 1989 ).**

Despite inconclusive evidence on its effectiveness in treating insomnia, L-tryptophan preparations have been used widely for inducing sleep as well as for the treatment of depression, obesity, and the premenstrual syndrome in addition to its use as adjuncts to physical fitness ( **Schneider-Helmert and Spinweber, 1986** ).

In fact, L-tryptophan use was advocated by physicians, psychologists, substance-abuse control centers, and weight loss programs ( **Silver, 1991** ). The presumed safety of L-tryptophan was based primarily on its status being natural or an essential amino acid ( **Mayer et al., 1990** ). In addition, no significant side effects had been reported with the use of L-tryptophan before the recognition of the eosinophilia-myalgia syndrome ( **Blauvelt and Falanga, 1991**).

It is interesting that in 1988, prior to the description of EMS, a clinical entity termed eosinophilic perimyositis had been reported which, in retrospect, was also associated with L-tryptophan ingestion ( **Silver, 1991** ).

The current surveillance definition of the Centers for Disease Control ( CDC ) of EMS requires fulfillment of three criteria; eosinophil count more than 1000 cells per mm3, myalgias of severity sufficient to interfere with a patient's ability to perform his or her usual activities, and exclusion of other infectious or neoplastic illnesses that might account for the first two findings ( **Kilbourne et al. , 1990** ).

The clinical features of the syndrome shows a wide spectrum and a great tendency for systemic involvement that may vary greatly from one patient to another ( **Shulman, 1990** ).

The spectrum of the reported clinical manifestations extends to include involvement of the pulmonary, cardiovascular, and central nervous systems. Approximately one half of the patients developed diffuse scleroderma-like cutaneous induration which on histopathologic examination showed marked thickening of the fascia and dermis caused by accumulation of collagen and mucopolysaccharides and accompanied by an inflammatory infiltrate of variable severity ( **Varga et al., 1992** ).

Most patients had striking peripheral blood eosinophilia in the initial phase of the illness. Bone marrow examination showed eosinophilic hyperplasia with normal precursor maturation. In contrast to many other disorders associated with eosinophilia, immunoglobulin E ( IgE ) levels were not elevated in the serum of EMS patients ( **Varga et al., 1993** ).

Although a large number of patients with the EMS are identified, the full clinical spectrum, natural history, optimal therapy, and long-term prognosis of this novel disease are still incompletely defined ( **Varga et al., 1993** ).

Despite the discontinuation of L-tryptophan use, a substantial proportion of patients developed a protracted course that was dominated by manifestations of cutaneous and neuromuscular involvement. Treatment with glucocorticoids

resulted in improvement of most of the acute manifestations of EMS and in rapid decrease in the peripheral blood eosinophil count. However skin induration, myopathy, and neuropathy responded poorly to this treatment **( Varga et al., 1992 ).**

The key unresolved issue regarding the EMS is the identity of the inciting agent. Other important but still unanswered questions concern the determinants of susceptibility to develop the syndrome after exposure to L-tryptophan, the cause of eosinophilia, and the relative roles of eosinophils and other inflammatory cells in causing tissue injury **( Martin et al., 1990 ).**

Elucidation of the exact etiology of the EMS may lead to the identification of an entirely new class of human toxicants and may also help to explain the causes of clinically similar disorders of obscure etiology, such as scleroderma **( Philen et al., 1993 ).**

Although the EMS outbreak has abated since manufactured tryptophan was recalled and withheld from public scale, questions regarding the appropriate regulation of vitamins and supplements remain unanswered. The EMS outbreak served to highlight the potential harm of products that can be advertised as natural, safe, and healthful.

# " EPIDEMIOLOGY OF EOSINOPHILIA-

# MYALGIA SYNDROME "

# EPIDEMIOLOGY OF EOSINOPHILIA-MYALGIA SYNDROME

In October 1989, physicians in New Mexico notified the New Mexico Department of Health and Environment of three female patients with marked eosinophilia and severe incapacitating myalgia. After thorough evaluation the illness seemed both unusual and obscure **( Blevins et al., 1989 ).**

The clinical picture in each of the three patients was that of a previously healthy woman in whom severe muscle pains and weakness, mucocutaneous lesions, and variable abdominal pain developed. Each one of the three patients had ingested 1.2 to 2.4 gram of L-tryptophan per day for three weeks to two and half years before becoming ill. None of the three patients had recently traveled outside the United States, none reported eating uncooked meat products, and none had had any recent symptoms of allergic disease. Their occupations were artist, homemaker, and restaurant hostess. None of their family members had any illnesses during this period. Although the three patients were taking various medications, an important early clue was the observation that the only medication shared by all of them was L-tryptophan **( hertzman et al., 1990 ).**

An article in a local newspaper resulted in a dramatic increase in reports to the New Mexico State Health Department. Subsequent case - control studies

in New Mexico and Minnesota established a statistically significant association between the ingestion of tryptophan and EMS ( **Hertzman et al., 1990** ).

Reports linking the use of L-tryptophan and the onset of EMS have prompted the Food and Drug Administration ( FDA ) to impose an automatic detention on L-tryptophan-containing products at United States' ports as a precautionary action **( Nightingale, 1990 ).**

Moreover, on November 17, 1989, the FDA recalled all dietary supplements that provided a daily dose of L-tryptophan equals or more than 100 mg. By March 22, 1990, this recall had been expanded to include all L-tryptophan-containing products at any dosage except some protein supplements, infant formulas and special dietary foods, and intravenous and oral solutions in which small amounts of L-tryptophan are needed for nutrient fortification **( CDC, 1990 ).**

Several methods were used to identify cases. Physicians and the public were alerted to the symptoms of EMS by a series of press releases from the Oregon Health Division. Persons with symptoms suggestive of EMS were urged to seek medical evaluation, and physicians were asked to report cases to the Oregon Health Division. Case reporting was directly solicited from all licensed physicians in Oregon through two state-wide mailings. Selected rheumatologists, pathologists, hematologists, and infectious disease specialists in the Portland metropolitan area were contacted by telephone and asked for