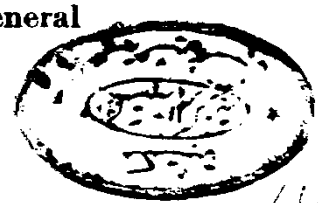
PROGRESSIVE SYSTEMIC SCLEROSIS (PSS)

ESSAY

Submitted in Partial Fulfilment for the Degree of Master of General Medicine



By

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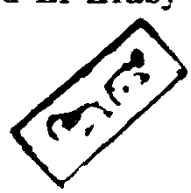

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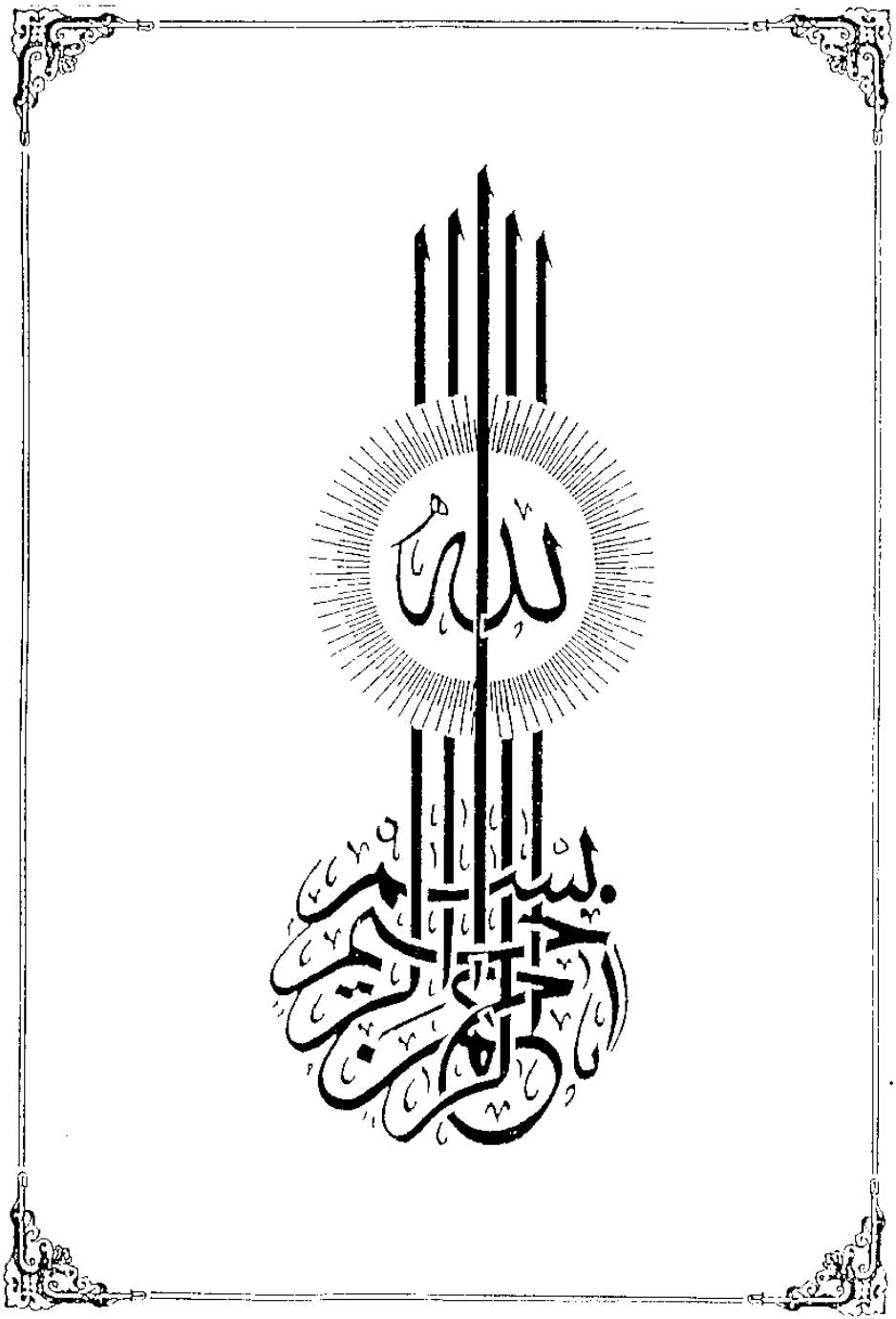

A C K N O W L E D G M E N T

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The Candidate.

C O N T E N T S

INTRODUCTION

Progressive systemic sclerosis (PSS), is a generalized disorder of connective tissue characterized by intense fibrosis and degenerative changes involving the skin, joints, blood vessels as well as internal organs especially the gastrointestinal tract; lungs, heart , CNS, eye and kidney.

Vascular lesions are a prominent features in PSS , the disease is variably severe and variably progressive, ranging from generalized cutaneous thickening(PSS with diffuse scleroderma) with rapidly progressive and fatal visceral involvement to a form that is characterized by restricted skin involvement often confined to fingers and face, and the passage of a prolonged period of time before the full expression of characteristic internal manifestation (CREST syndrome variant).

The etiology of PSS remains obscure, recently there are a variety of abnormal serologic and cellular immune reaction in a significant number of patients has suggested that immunologic mechanisms are important in its pathogenesis. There are a close relationship between PSS and other connective tissue diseases especially SLE, polymyostitis and mixed connective tissue disease.

HISTORIC BACKGROUND

Early descriptions of PSS are credited by Lewin and Heller (1859) to Zacutus lusitanus in 1634, to Diemerbroeck in 1660, and to Curzio of Naples in 1752.

In 1847 Gintrac is believed to have been the first to use the term "scleroderma" and referred to Forget's use of the term" cutaneous sclerostenosis".

One of two other reports which appeared in the French literature the same year was prepared by Grisolle (1847).

Also Forget (1847) described a 38-year-old woman whose initial symptoms were pain and swelling of joints Raynaud (1862) was familiar with hardening of the skin on the extremities which accompanied the phenomenon of local asphyxia he described in 1862 and which is recognized by the eponymic term "Raynaud's phenomenon".

Addison (1868) described two cases of "Keloid" or "scleriasis in a posthumous collection of his writings publish in 1868, conditions, which would surely be identified now as the advanced changes of scleroderma.

In 1878, Weber attributed subcutaneous deposits of calcium in patients with scleroderma to a form of gout.

In 1889 Finlay observed significant limitation of pulmonary expansion in a male with scleroderma and is credited with the recognition of the association of scleroderma and pulmonary fibrosis.

In 1896 Hutchinson called attention to the hardening of the skin on the extremities of a patient, a condition which he identified as "acroscleroderma".

Dercum (1896) noted, roentgenographically , narrowing of the proximal and distal interphalangeal joints in the hands of a patient with scleroderma.

The esophageal disturbance of scleroderma was reported first by Ehrmann in 1903, in 1910 Thibierge and Weissen bach emphasized the clinical entity of calcinosis with scleroderma. The eponymic term "Thibierger-Weissenbach Syndrome " is sometimes employed to identify this late manifestation of the disease.

In 1931 Rake reported pathologic findings in the small bowel. Masugi and Ya-Shu (1938) observed fibrinoid changes in the blood vessels of a patient with scleroderma and suggested that an allergic reaction was responsible for the structural alterations.

In the same year Atkinson and Weber prepared an excellent historic summary of the general subject of calcinosis, in 1945 Goetz proposed the term. "Progressive systemic sclerosis" as a preferred substitute for generalized scleroderma, this is the acceptable term in current use, since PSS is characteristically progressive in course and the sclerosis is systemic as it extends beyond the skin and may involve most of the internal organs.

CLASSIFICATION OF SCLERODERMA

The term scleroderma applied not only to the cutaneous changes of PSS, but to a heterogeneous group of conditions in which there is more circumscribed or patchy sclerosis of the skin, the hardening, tightening and inelasticity of the integument may be indistinguishable from that observed in PSS, but certain pathologic as well as clinical differences exist between these conditions and PSS.

In a recently completed multicenter cooperative study 799 patients with early PSS and certain closely related disorders were examined prospectively for the purpose of developing criteria for the classification and separation of these diseases (Masi, A.T.; Rodnan, G.P., 1978).

In this large series of patients, sclerodermatous skin changes proximal to the digits was the most powerful single criterion (91% in individual with definite PSS, compared with 10% in control subjects), an additional set of findings was proposed as secondary or minor criteria including sclerodacyly, digital pitting scars, bilateral basilar pulmonary fibrosis and colonic sacculations.

An additional 7% of individuals considered to have definite PSS without proximal skin changes had at least two of these four findings, compared with only 2% of controls.

Table 1-Classification of Scleroderma

1	[illegible] sclerosis
	a. With characteristic diffuse involvement of the skin (scleroderma)—affecting trunk, face, and proximal as well as distal portions of the extremities, and a tendency toward the relatively early appearance of disease of the esophagus, intestine, heart, lung, and kidney—(classic [illegible])
	b. With relatively limited involvement of the skin—often confined to the fingers and face, predominance of calcinosis, Raynaud's phenomenon, esophageal dysfunction, sclerodactyly, telangiectasia, and prolonged delay in appearance of distinctive internal manifestations (usually severe pulmonary arterial hypertension and biliary cirrhosis), i.e. the CREST syndrome
	c. Overlap syndromes, including sclerodermatomyositis and mixed connective tissue disease
2	Localized (focal) forms of scleroderma
	a. Morphea
	1. Spots or multiple plaques
	2. Generalized morphea
	b. Linear scleroderma, with or without melorheostosis
	c. Scleroderma en coup de sabre with or without facial hemiatrophy
3	Miscellaneous sclerotic or scleroderma-like conditions
	a. Progressive systemic disease
	b. Nodular calcific fibrosis
4	Eosinophilic fasciitis

Using these criteria in combination, 98% of patients with PSS met one or the other compared with only 3% of controls (98% sensitivity and 97% specificity).

Generally scleroderma classified into the following:

1- Progressive systemic sclerosis :

A- With symmetric, diffuse involvement of the skin (scleroderma)-affecting trunk, face and proximal as well as distal portions of the extremities, and a tendency towards the relatively early appearance of disease of the esophagus, intestine, heart, lung and kidney-this is the classic disease.

B- With relatively limited involvement of the skin, often confined to the fingers and face, prominence of calcinosis, Raynaud's phenomenon, esophageal dysfunction, sclerodactyly, telangiectasia and prolonged delay in appearance of distinctive internal manifestations (including severe pulmonary arterial hypertension and biliary cirrhosis), this is the CREST syndrome.

C- "Overlap" syndromes, and this include scleroderma-tomyositis and mixed connective tissue disease(features of systemic lupus erythematiosus, scleroderma and polymyositis).

2- Localized (Focal forms of Scleroderma :

A- Morphea: this variety begins with areas of erythematous or violaceous discoloration of the skin, which take the form of discrete drop-like patches(guttate morphea) or plaques :

a- Single or multiple plaques.

b- Generalized morphea.

B- Linear scleroderma, with or without melorheostosis is this form of scleroderma, a linear streak of sclerosis appears in the upper or lower extremity, or in the fronto-parietal area of the forehead and scalp (en coup de sabre).

C- Scleroderma en coup de sabre, with or without facial hemiatrophy.

3- Drug-Induced Scleroderma-Like Conditions :

A- Polyvinyl chloride disease :

Small percentage of workmen who clean reactor-vessels containing polyvinyl chloride develop sorneness and tenderness of finger tips, Raynauds phenomenon, induration of skin, synovial thickening of the proximal interphalangeal joints, hepatic portal fibrosis and pulmonary fibrosis.

B- Bleomycin-Induced Fibrosis :

Administration of the tumoricidal drug often leads to the development of nodules and or plaques of thickened skin closely similar to that found in PSS, occasionally generalized induration, of the skin, pulmonary fibrosis and Raynaud's phenomenon occurs with this drug, closely similar to naturally occurring PSS.

4- Eosinophilic Fascitis :

Shulman (1975) describe a scleroderma-like discroder chiefly affecting adults, onset with pain, swelling and tenderness of the hands, feet and legs soon followed by the development of severe induration of the skin and

subcutaneous tissues with marked limitation of motion of hands and feet, flexion contractures of the fingers occurs, carpaltunnel syndrome is an early features in many cases, the induration may remain confined to the extremities or spread to affect trunk as well as the face, Raynaud's phenomenon and internal manifestations of PSS are absent, striking peripheral eosinophilia is present during early stages and hypergammaglobulinaemia (IgG) is common.