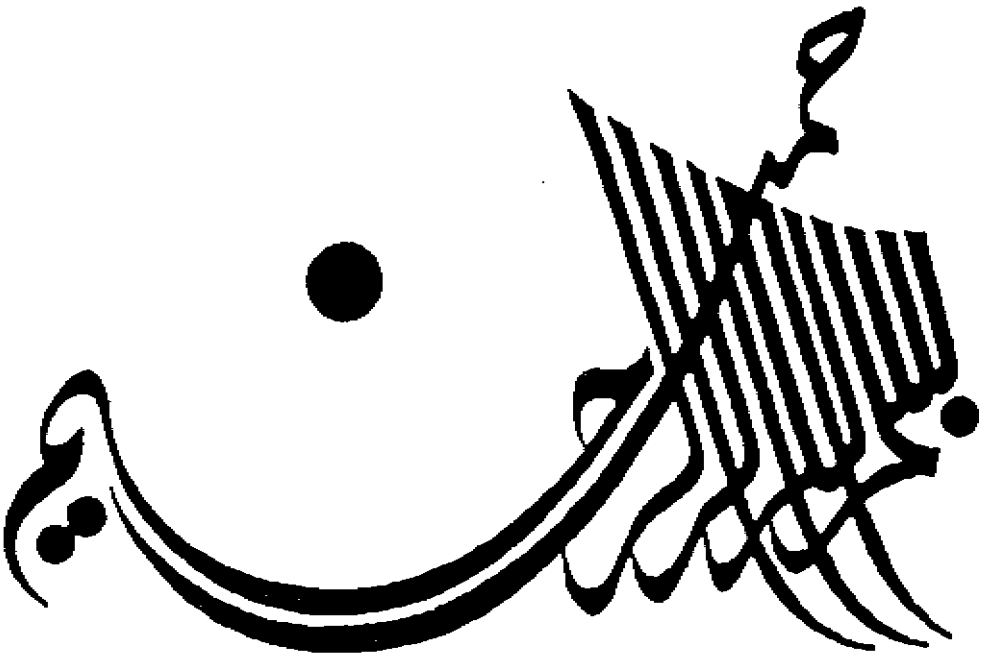

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PATHOLOGICAL STUDY OF CARDIOMYOPATHY

THESIS

Submitted for Partial Fulfillment of
The Master Degree of Pathology

By

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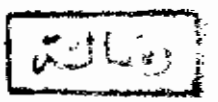

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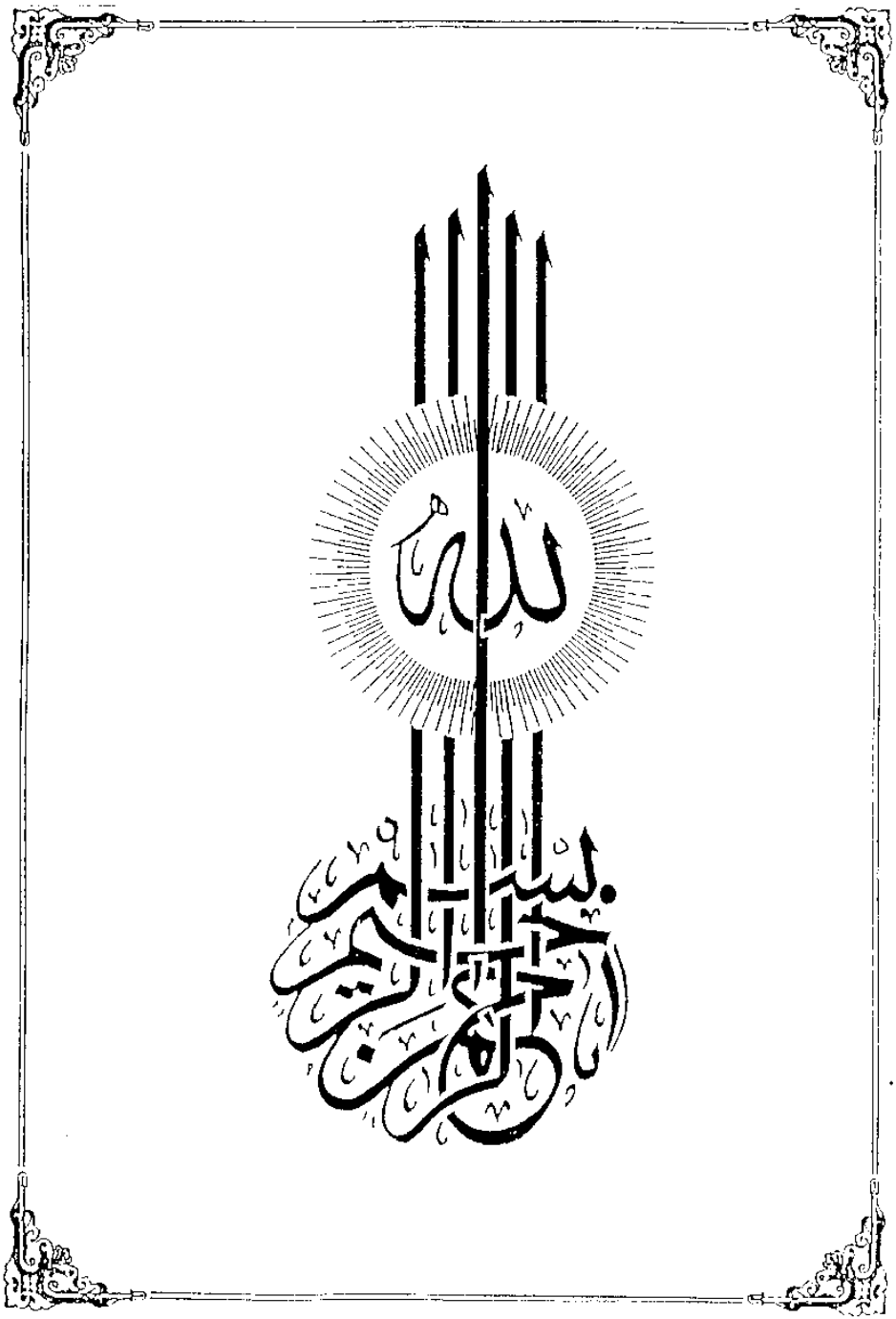

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CONTENTS

List of Abbreviations Used

ANP	: Atrial natriuretic polypeptide
ASH	: Asymmetric septal hypertrophy
DC	: Dilated cardiomyopathy
DST	: Disproportionate septal thickening
EFE	: Endocardial fibroelastosis
EMF	: Endomyocardial fibrosis
HC	: Hypertrophic cardiomyopathy
HLA	: Human leukocyte antigen
IHSS	: Idiopathic hypertrophic subaortic stenosis
ISFC	: International Society and Federation of Cardiology
LVEF	: Left ventricular ejection fraction
PAS	: Periodic acid-Schiff
PPCM	: Peripartum cardiomyopathy
triac	: Triiodothyroacetic acid
WHO	: World Health Organization

INTRODUCTION AND AIM OF THE WORK

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Although much has been written on the various cardiomyopathies, surprisingly few reports have focused on the pathological anatomy of these conditions (*Roberts and Ferrans*, 1974).

The lack of knowledge of the factors determining the histologic alterations of the heart and of the pathophysiologic mechanisms conditioned by the structural changes of cardiac tissue has led to much confusion about primary cardiomyopathies (*Anselmi et al.*, 1975).

The history of cardiomyopathies over the past three decades is briefly surveyed and the definition of cardiomyopathy as "heart muscle disease of unknown cause" is reaffirmed. The recent slight modification of the classification based on disorders of structure and function into dilated (congestive), hypertrophic and restrictive/obliterative cardiomyopathy is underlined (*Goodwin*, 1982).

The aim of this work is to throw a spotlight on the pathology of the different types of idiopathic cardiomyopathy including the recent theories in its etiology and pathogenesis. To fulfill this aim, a review of literature is aimed at.

REVIEW OF LITERATURE

THE STRUCTURE OF THE WALL OF THE HEART
[*Van Der Bel-Kahn*, (1977) & *Cormack*, (1987)]

The wall of the heart is formed mainly of the myocardium which is covered on the outside and inside by two membranes: The epicardium and the endocardium.

The Myocardium

Is typically classified into three muscle layers: The superficial (subepicardial) and the middle and the deep (subendocardial). The intertwining of muscle bundles is apparently not intricate enough to prevent the unfolding of the different muscle layers. The direction of the muscle fibers differs in each of the three layers but, within the confines of each layer, the myocardial fibers are apparently arranged parallel to each other. The cardiac muscle fibers which are separated by endomysium and show extensive branching and anastomosing are made up of short cylindrical muscle cells with central oval nucleus. The cells are interconnected end to end by intercalated disks that include gap junctions.

The Endocardium

This connective tissue membrane forms a complete lining for the atria and ventricles and covers all the structures projecting into them, such as valves, chordae tendineae, and papillary muscles. In general, the

thickness of the endocardium varies inversely with the thickness of the myocardium it lines. The endocardium consists of three layers: Innermost layer of endothelium, a thick middle layer of dense connective tissue rich in elastic fibers and an outermost layer of loose connective tissue which is continuous with the endomysium of the myocardium and contains blood vessels and Purkinje fibers.

The Epicardium

Is the visceral layer of the double-layered pericardium, which invests the heart from the outside. It is formed of a layer of simple squamous epithelium with an underlying subserous layer of connective tissue which contains coronary vessels and fat cells. The connective tissue blends with the endomysium of the myocardium.

Development and Calculation of the Interventricular Septum Thickness

The normal embryonic septum is about twice as thick as the ventricular free wall when it first forms as an infolding of the cardiac tube. Throughout subsequent embryonic and foetal cardiac development there is a gradual reduction in the ratio of septum-to-left ventricular free wall thickness until about the time of birth, when it is at the normal ratio of 0.94 (*Hutchins and Bulkley*, 1978).

In 180 consecutive healthy subjects studied by *Bentivoglio et al.* (1989), a stepwise multiple regression analysis (with age, weight, height

and systolic and diastolic blood pressure as independent variables) yielded the following equation:

$$\text{Septal thickness (mm)} = 0.019 \times \text{SBP} + 0.04 \times \text{W} + 2.74$$

where SBP = systolic blood pressure (mm Hg)

W = weight (Kg)

Thus systolic blood pressure and weight, but not the age, were independent determinants of interventricular septum thickness in apparently healthy subjects. The association between interventricular septal thickness and age described by *Milne and colleagues* (1989) could be the consequence of the relation between wall thickness and blood pressure, which increases with age.

CARDIOMYOPATHY

Definition and Classification

Three decades ago the frontiers of cardiomyopathy were ill-defined and nebulous because no working definition or classification had been suggested and delineation was imprecise. The cardiomyopathies were often confused with myocarditis, a term used widely in a variety of pathological and clinical contexts without clarity of expression: Myocarditis was sometimes equated with cardiomyopathy, sometimes with a specific inflammatory disorder (*Goodwin*, 1982).

In 1957 *Brigden* published his lecture on "Uncommon myocardial diseases; the non-coronary cardiomyopathies". *Brigden* pointed out the diversity of the disorder and the difficulty of classification and was among the first to use the term "Cardiomyopathy". Not surprisingly he regarded the cardiomyopathies as rare disorders which indeed they seemed to be at that time.

In 1961 *Goodwin et al's* first paper was published defining cardiomyopathy and attempting a classification. The definition was inaccurate but was slightly modified in a subsequent paper on cardiac function in primary myocardial disorders as follows: "Cardiomyopathy: an acute, subacute or chronic disorder of heart muscle of unknown or obscure aetiology, often with associated endocardial or sometimes with

pericardial involvement but not atherosclerotic in origin" (*Goodwin*, 1964).

At this time it was suggested that the term "primary myocardial disorder" should be used to describe those cardiomyopathies that were not the result of diseases in other parts of the heart or elsewhere in the body; subsequently, in conjunction with *Dr. Celia Oakley*, the definition of cardiomyopathy was simplified to "a disorder of cardiac muscle of unknown cause" while myocardial disorders that were part of a general systemic disease were termed "rare specific heart muscle diseases". Thus automatically any condition of which the cause or pathological process could be defined clearly was excluded from the definition of cardiomyopathy (*Goodwin and Oakley*, 1972). This concept has not always been readily accepted but received approval from the joint task force of the World Health Organization and International Society and Federation of Cardiology on the definition and classification of cardiomyopathies (*WHO/ISFC*, 1980).

Cotran et al. (1989) classified cardiomyopathy into two main types, primary cardiomyopathy and secondary cardiomyopathy. Primary cardiomyopathy refers to heart muscle diseases of unknown cause while secondary cardiomyopathy refers to those myocardial disorders of known cause, excluding ischemic, hypertensive, valvular, pericardial, congenital, and inflammatory involvements.

PRIMARY CARDIOMYOPATHY

Classification

The concept of a classification based upon the disorders of structure and function was introduced in 1964 when it was suggested that cardiomyopathies might present clinically in one of three ways: As congestive, constrictive or obstructive types, respectively (*Goodwin*, 1964).

Subsequent work has shown that these types are distinct entities that do not merge from one into the other. It has also been recognized that the "obstructive" type is notable mainly for massive ventricular hypertrophy and impaired diastolic function. The definition was revised to "hypertrophic obstructive cardiomyopathy" when it was realized that massive hypertrophy was a cardinal feature of the disease. At this time it was generally agreed that obstruction to the outflow of the left ventricle was an important feature of the condition, though it had been recognized that in some patients no such obstruction existed (*Cohen et al.*, 1964).

The importance of obstruction was first questioned by *Criley et al. in* 1965 and by *Swan et al.* in 1971 who noted that as the disease became more severe, the signs of obstruction tended to disappear. Since then, the evidence for true obstruction has become significantly less (*Goodwin*, 1974).