STUDIES ON THE EFFECTS OF AGE ON THE HEART

THESIS
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[PHYSIOLOGY]

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MEMORANDOM

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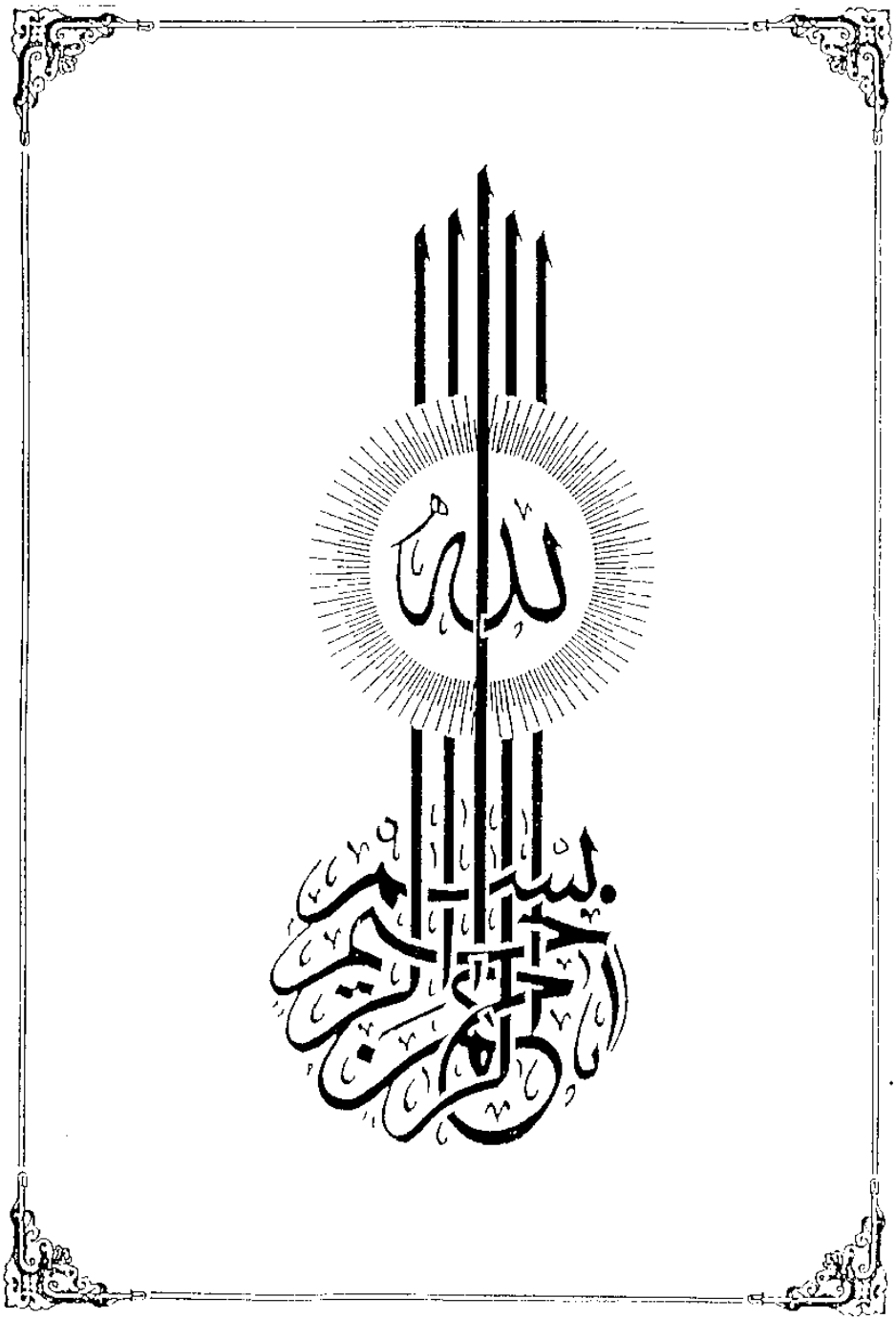

" بسم الله الرحمن الرحيم "

الحمد لله الذى هدانا لهذا وما كنا
لنهتدى لولا أن هدانا الله ..

سوره الاعراف
الآيه رقم (٤٣)

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CONTENTS

INTRODUCTION

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One of the systems, mostly showing changes with age is the cardiovascular system. The structural changes that occur with ageing may, produce little or no functional effects at rest. However, with various stresses, the capacity of the cardiovascular system to adapt is impaired with advancing age, and may thus underly the failure of the aged subjects to survive stress.

Despite considerable efforts done, there is still no clear consensus as to the intrinsic alterations in the heart as a function of age.

The process of ageing refers to the changes that occur with the passage of time throughout the whole lifespan. However the term ageing is usually coined with the very late or senescent period of life, to which most of the studies are directed.

A common problem in studying the effect of age in the heart during senility is the difficulty in dissociating the true effect of ageing from those due to the conditions that usually accompany senility such as

coronary artery disease and deconditioning of the heart due to sedentary life style.

It was important therefore to undertake this study in the presenescent stage of life, before the development of the pathological changes associated with senescent stage.

AIM OF THE WORK

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The present study was planned in order to establish the age induced changes in the norms of cardiac function as regards both chronotropy and inotropy.

A Langendorff preparation of isolated perfused hearts was chosen in order to exclude the effects of various factors that might influence in vivo studies such as anesthesia , respiratory movement, cardiovascular reflexes and neural or hormonal factors.

In addition such preparation perserves the normal geometry of myocardial muscles fibers and enables transport of substrats and circulating factors to myocardial cells through the normal physiological channels by intact coronary circulation.

Adoption of such technique also allows for the study of intrinsic activity, both under basal conditions and following beta-adrenergic stimulation by isoproterenol infusion.

REVIEW OF LITERATURE

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Definition of ageing:

Of the many definitions given for ageing, the ones presented here are selected on basis of their relevance to the physiologic aspects of ageing. Although it is commonly associated with changes acompanying senesence, ageing in the strict sense of the word means change with age during any of the three stages of the lifespan of the organism, namely the postnatal, the adult or reproductive and the senescent stage **(Rakusan, 1984).**

Also, focussing on ageing as a stage of the lifespan, **Timiras (1988)** defined ageing as the sum of all changes that occur in an organism with the passage of time.

In the mean time, ageing may be viewed as a deteriorative process characterized by increased vulneriability and decreased viability. Thus ageing takes the form of morphologic and functional involution, always progressive and often silent, affecting most organs, tissues and cells, and resulting in gradual decline in performance leading to functional impairment and death **(Timiras, 1988).**

A major function which progressively fails with ageing is the capacity for adaptation to environmental stresses. Ageing may, therefore be defined as the decreasing ability to survive stress. The ultimate failure of such physiologic processes necessary to sustain homeostasis, that is to maintain a constant milieu interieur, results in death.

Other definitions of ageing, also given by **Timiras (1988)**, focused on cellular and molecular changes. Thus ageing and death would result from progressive cellular changes in the plasma and intracellular membrane (fluidity, permeability and transport.) cytoplasm (formation of free radicals, cross linking and Lipofuscin) and nucleus (DNA damage and DNA repair failure).

Theories of ageing :

Many theories were suggested in order to explain the phenomenon of ageing on basis of systemic, cellular and molecular events **(Sharma , 1988)**.

I. **Systemic theories**:

Systemic theories ascribe ageing of entire organism to decrements in the function of a key system, such as the nervous, endocrine and immune systems. Such

decrements could be genetically programmed. Alteration in the key system will generate changes throughout the entire organism. For efficient adaptation, nervous and endocrine signals must be synchronized and responsive to the need of many functions they regulate (**Timiras, 1978, 1985**). However, with ageing. Some of the efficiency of the hypothalmopititary signals is lost or altered (**Everitt and Burgess 1976**). This results in decreased function and increased pathology of most organs and tissues.

Systems according to this theory, command neurons in higher brain centers would act as "Pacemakers" that regulate the "biologic clock" that governs development and ageing. With the passage of time, ageing changes may result from programmed deterioration or cessation of the programming that regulate homeostasis (**Walker and Timiras, 1982**). In either case, ageing would be manifested through a slowing down or imbalance in the activity of the pacemaker neurons with consequent neurotransmitter and hormonal alterations.

II. Cellular theories:

These theories are related to the changes that