ADRENAL RESERVE IN AGING

Thesis

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By

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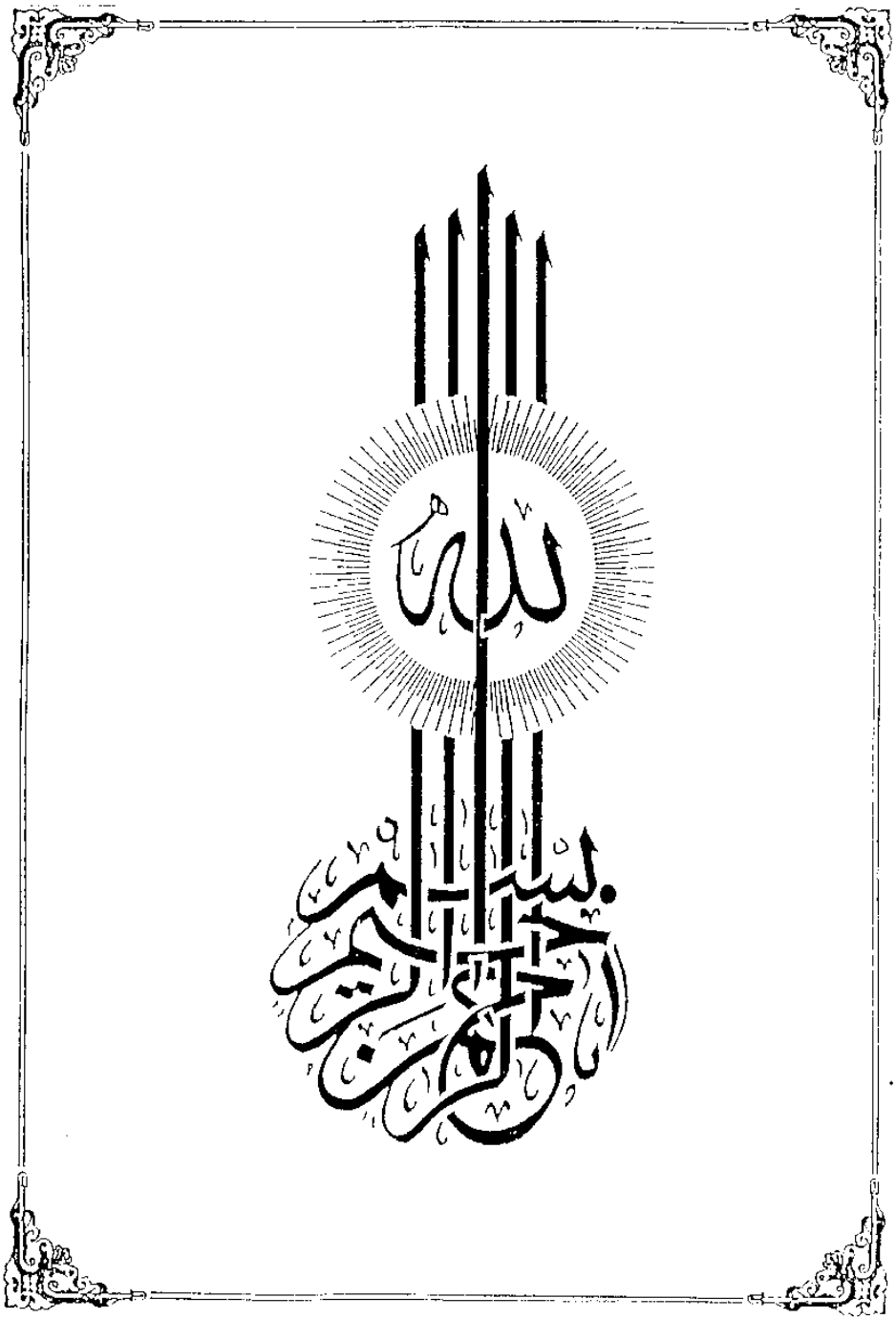

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CONTENTS

INTRODUCTION AND AIM OF THE WORK

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It has long been of interest whether or not aging alters the ability of adrenal cortex to response to adrenocorticotrophin (ACTH).

Several studies have shown that the increase in plasma cortisol shortly after a submaximal dose of ACTH is unchanged in old age (Blichert-Tifr et al., 1970 and Vermerullen et al., 1982). However this does not imply that the aged adrenal continues to response normally to low doses of ACTH.

Age was thought by some scientists to be the direct result of deficiency states resulting from age related insufficiency of the endocrine glands.
Few is known about the adrenal reserve to ACTH in advanced age.

The aim of this mork is to study the adrenal reserve in different age groups from 20 to above 60 years old and its response to ACTH 250 ug I.M. in those age groups.

REVIEW OF LITERATURE

AGING

Definition:-

The terms aging and senescence are familiar and there is no general agrement among geronotologists about how they should be used usually senescence is used when we talk about the changes that occur during the period of obvious functional decline in the later years of an animal's life span. Some people use the term aging for the same processes and period others use it in a much more general way with aging meaning simply growing older and its changes being any changes related to age regardless of when in the life span they occur. In fact the terms aging and senescence are frequently used interchangeably. It is worth to emphasize the following points. Primarily the changes which occur during aging are deleterious, they increase the chances that an animal will die. Aging therefore involves a decrease in the ability of an animal to cope with its environment secondarily the deleterious-age related changes are cumulative. Death the ultimate result of aging is sudden, but the process of aging involves a progressive increase in the probability of dying. Thirdly the age related processes involved are common to all members of a species and are inescapable consequences of getting older. That is to say

aging and senescence are fundamental intrinsic properties of living organisms (Lamb, 1977).

It has long been a debatable question as to whether aging studies should include those changes which precede the degenerative changes of old age some workers have suggested that aging commences at conception and therefore that growth maturation and senescence represent a contrnum without any major discontinuity others contend that the aging process is a discrete phenomenon only apparent in advanced age and should be treated separately from the developement phases. Senescence is a general term for a decrease in the efficient functioning of an organism with increasing age senescent changes can occur at any stage in the life process. It may be possible to state a composite statement with the following elements.

1) Aging may be apparent throughout life but is more noticable in the post-reproductive period; (2) Aging lowers the functional capacity of cells, organs and entere organism (3) Aging results in the degradation of structural elements within the body (4) Aging lowers the effectiveness of the response of the organism to internal and external factors and (5) Aging increase the likelihood of the ultimate disfunction death (Hall, 1982).

One of the most important facts is that different species have different characteristic life-spans. As each animal species has its own characteristic life-span and since what determines whether an animal belongs to one particular species or another is its genetic constitution it must follow that genetic differences are responsible for the differences in the longevities of different species life. Gradually a fairly consistent body of evidence was built up which showed that there was a positive correlation between the life-spans of parents and children. If as the evidence suggests there is a correlation between the life-span (longevity) of parents and children is it proof of a genetic component in longevity? "No" is the answer to this question because environmental factors could be the cause of the correlation. For example, infecious diseases such as tuberculosis can be transmitted from parents to children could influence the life spans of both in a similar way parents and children are more likely to share the same occupation and occupational hazards than unrelated people and this will tend to make there life spans more similar parents and children are likely to have similar eating habits and if longevity is affected by diet this will mean that their longevities will tend to be more close than those of unrelated people. Twin studies have suggested that hereditary factors are important in determing longevity by

findings that showed that the life-spans of monozygotic twins are more similar than those of dizygotic twins. Nevertheless it is well known that there may be reasons not directly related to their genetic similarity which may be why monozygotic twins are more similar than dizygotic twins. A number of people have stated that in most species. The female sex outlives the male. This is certainly true in man many suggestions have been made for what is the reason for this difference and no really satisfactory explanations seen to have been made (Lamb, 1977).

According to one current classification the elderly are people between 60 and 74 years old. The aged are those over 75 years old including the longevous of 90 years and more (Frolhis, 1975).

A basis for a new terminology is the technical life span of man. This age i.e. the oldest age to which a number of human is documented to have lived is 115 years old. For persons 86 years and older in the last quarter of the technical life-span of man the term aged is appropriate. The term elderly is applied to those 77 througs 85 years who have survived at least two thirds of the technical life-span of man. Aging describes those 69 through 76 years who have survived at least three fifths of the technical life span of

man. Persons 68 years and below would be categorized as mature adults (Watkin, 1982).

Little is known about the origins of senescence and little agreement exists regarding the true nature of the aging process (Goldstein, 1977).

There is no general agreement about the fundamental cause or causes of aging although there are many different ideas about how and why it may happen, no single theory is capable of explaining the facts of aging (Lamb, 1977).

Hence the change in the modern life is not an increase in the upper limit of the human life span but it is an increase in the proportion and number who survive to approach that limit. This trend is the result of a narrowing of the gap between primary aging, which is genetically determined and immutable and secondary aging which is attributable to personal, social and environmental factors that may be subjected to change only when reduced to the simplest unit of organization the cell can be studied independently of age related disease. Even at this level knowlege about aging is primitive, and several theories of aging remain extant (Hazzard, 1987).

Aging of cells and tissues in vivo:

During the course of development, cells become specialized for different functions. It is convenient to use a rather simple scheme of classifying the cell types in the body based on both the extent of differentiation and the capacity of the cells to divide; (1) Fixed post mitotic cells they are the final products of differentiation. They are highly specialized for particular functions and are incapable of all division. Nerve muscle and red blood cells are examples of this cell type, (2) Reverting post-mitotic cells also highly specialized but although they are fully differentiated they are still capable of division but usually they do not divide frequently but they can do so. Examples of this cell type are liver and kidney cells; (3) Stem cells are less specialized cells which readily undergo cell division. The basal cells of the epidermis come into this category. They are partially differentiated cells. Some prefer the term progenitor cell to stem cell.

The different tissues and organs of the body vary with regard to the types of cell found on them some tissues such as the epidermis and intestinal epithelium are constantly being renewed.

In these renewable tissues cell division occurs in a growth zone and as the products of division move away from the germinative region they differentiate and mature. Ultimately the fully differentiated cells die and are sloughed off. Tissues such as the liver do not contain stem cells. Normally, cell division is rare but if cells are damaged or destroyed the differentiated cells are capable of dividing and restoring the tissue. This type of tissue is referred to as an expanding tissue striated muscles and nervous tissue are non renewable tissues, since they contain mainly fixed post-mitotic cells. It the tissues are damaged or partially destroyed they are not replaced.

There is no type of cell or tissue that is unaffected by age although the nature of the changes seen depends on tissues being studied.

For non-renewing tissues e.g. nervous, there is some evidence that long lived fixed post-mitotic cells decrease in number and that changes within the cells e.g. Lipofuscin accumulation might affect their ability to function normal. Deterioration in the quality and quantity of the cells in these tissues could therofore cause the functional decline in the whole animal.