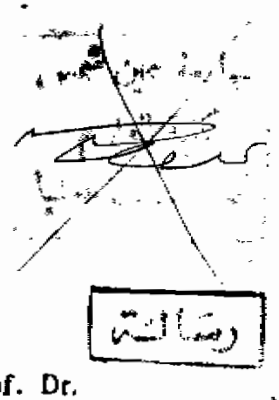
THYROID FUNCTION IN MALE INFERTILITY

THESIS

in Partial Fulfillment for Requirement of
The Degree of M. Sc. in Biochemistry



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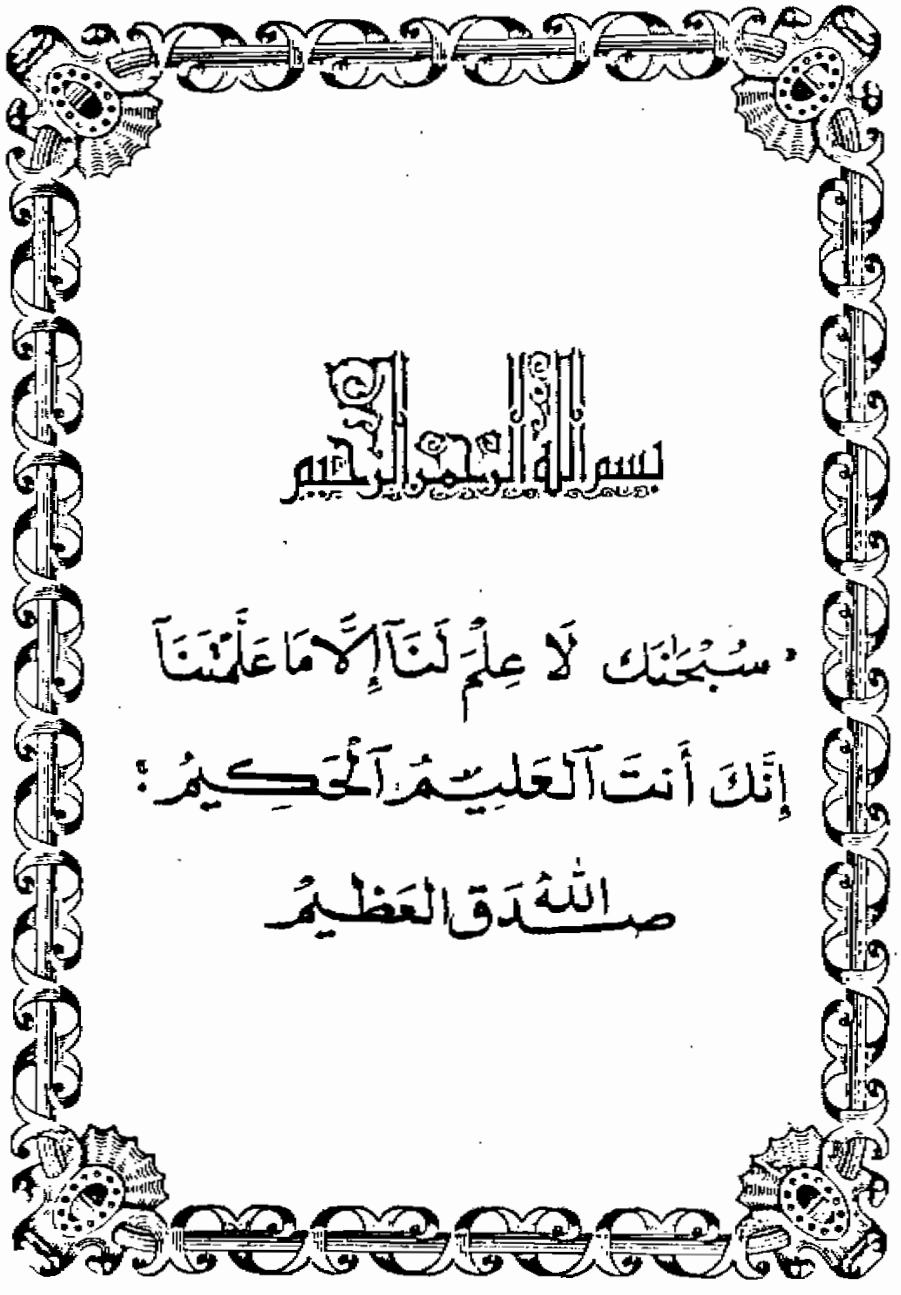

بسم الله الرحمن الرحيم

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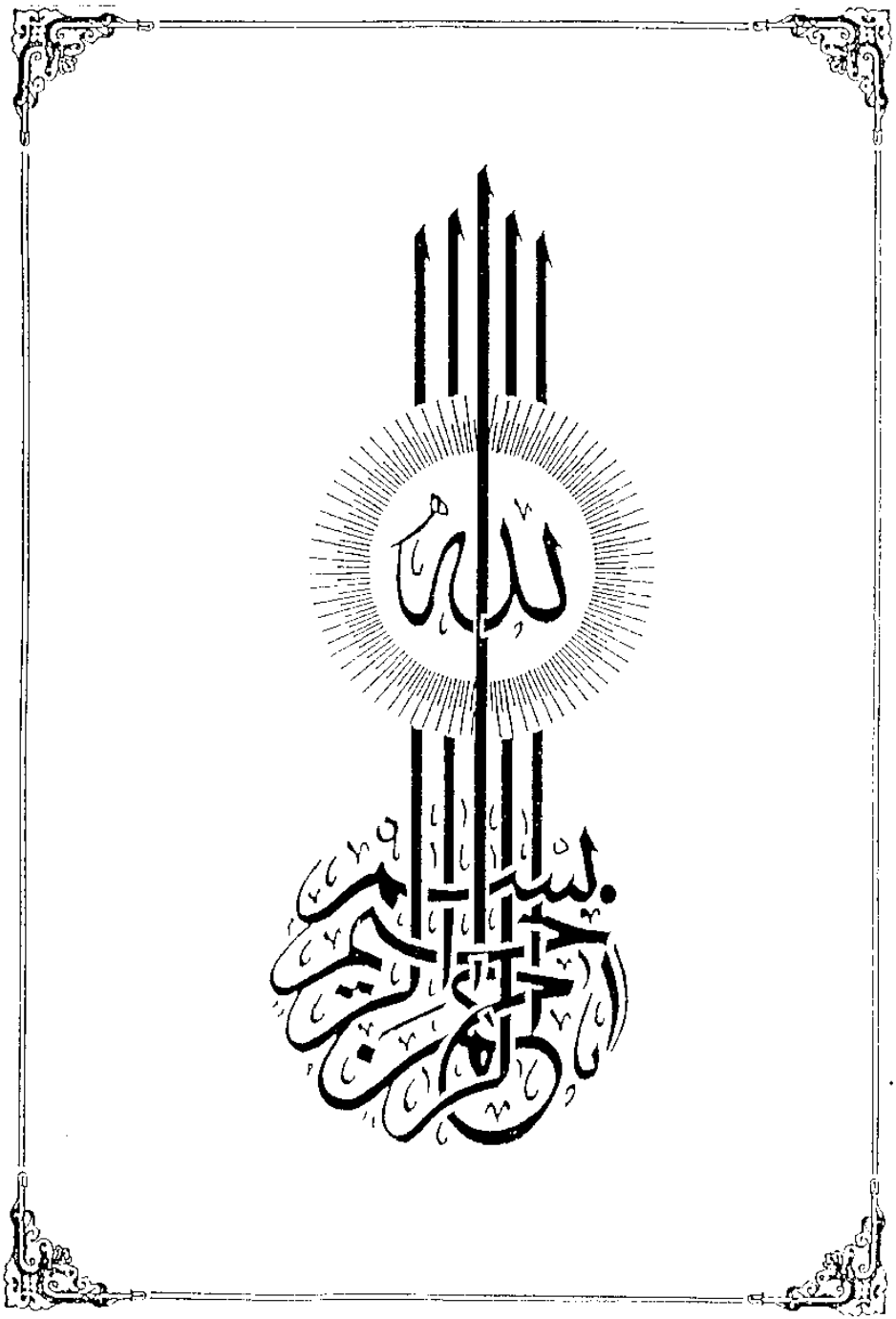

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CONTENTS

ABBREVIATIONS

F.S.H. = Follicle stimulating hormone.

CAMP = Cyclic 3,5 adenosine monophosphate.

DNA = = Deoxy ribonucleic acid.

RNA = ribonucleic acid

ABP = androgen binding protein.

ATP = adenosine triphosphate.

TSH = thyroid stimulating hormone (thyrotropin)

MIT = monoiodotyrosine.

DIT = Diiodotyrosine.

T_4 = tetraiodothyronine (thyroxine)

T_3 = triiodothyronine.

rT_3 = reversed triiodothyronine.

mRNA = messenger ribonucleic acid.

tRNA = transfer ribonucleic acid.

TBG = T_4 binding inter α globulin.

TBPA = T_4 binding prealbumin.

Ig = immunoglobulin.

TRH = thyrotropin releasing hormone.

LDL = Low density lipoprotein.

LH = Leutinizing hormone.

RAIu = radioactive iodine uptake.

A/G = Albumin globulin ratio.

GMP = Guanosine monophosphatase.

Ca^{++} = Calcium.

Na^{+} = Sodium.

K^{+} = Potassium.

Zn^{++} = Zinc.

Cu^{++} = Cupper.

Pb^{++} = lead.

Hg = mercury.

Mg^{++} = Magnesium.

Ca^{++}ATPase = Calcium Adenosine triphosphate

hcG = human chrionic gonadojrophin.

RIA = radio immunoassay.

GH = growth hormone.

t = test of significane.

P = probability test.

PART I

INTRODUCTION AND AIM OF THE WORK

INTRODUCTION

Fertility and infertility, has been a matter of socioeconomic debate. In growing countries control of fertility is required inspite of social trend against such an issue.

Andrologists comprehend the complicated problem when they attempt to get an overview of spermatozoal fertilizing capacity by sperm count, morphology, motility, and semen volume, plus or minus a variety of other parameters that laboratory may assess (Bain et al., 1982).

As infertility is the failure of reproduction, male is responsible for about 40% of infertility (Ghalioungui and Ghareeb, 1978).

The function of the testes begins with onset of puberty. At puberty the testis undergoes maturational changes and the leydig cell increases it's activity and sensitivity to gonadotropin by increasing it's testosterone secretion. So the main function of the testes include two main processes which are spermatogensis and steroidogenesis. Spermatogenesis is the elaborate cytological process by which a spermatogonial stem cell produces the

spermatozoa. This process of cell differentiation takes place within the seminiferous tubules of the testes.

(Steinberger, 1975) Proposes the following chain of molecular events:-

1. FSH binds to sertoli cell membrane receptors, and there it activates adenyl cyclase which stimulates synthesis of cAMP which promotes DNA dependent RNA synthesis resulting in the formation of a number or protein including a testicular androgen binding protein (ABP).

ABP which is secreted by sertoli cells enters the intercellular spaces of semineferous epithelium. The ABP-androgen complex comes in contact with germ cell membrane where it facilitates the transfer of the androgen to a cytoplasmic androgen receptor.

The receptor androgen complex is transported into the germ cell nucleus (Steinberger, 1975).

Spermatogenesis can be divided into three phases:-

The 1 st phase: most of the spermatogonia proliferate to give rise to spermatocytes, while the remainder maintains their own number by renewing themselves (Clermont and Antar, 1973).

The 2 nd phase: involves the primary and secondary spermatocytes that go through a process of reductional division leading to the formation of spermatids (Ganong, 1979),

The 3 rd phase: The spermatids go through a complex of metamorphosis leading to the production of highly differentiated motile cells spermatozoa.

In humans, it takes an average of 74 days to form a mature sperm from primitive germ cell (Ganong, 1983).

It has been found that there are some factors which affect infertility in male one of them is the excessive temperature in the scrotal region which can adversely alter spermatogenesis (Cockett and Ronald, 1976). The suggestion has been made that cooling and possibly alternating warm and cold treatment may result in increased spermatogenesis and possibly have value in improving the prognosis of severe of oligospermia.

There are a number of drugs that alter spermatogenesis either by inhibiting the completion of the development of mature spermatozoa or by rendering them incapable of fertilization.

Also sometimes in the early embryo, the gonads is bipotential structure with the capacity to differentiate into the testis or ovary. The medulla of this primordial gonad becomes a testis if the chromosomal constitution of the germ cell carries (Y) chromosome (Cockett and Roland, 1976).

In Pseudo-hermaphrodi- tism the gonads are of one type, either testicles or ovaries, but the external genilalia and somatic appearance belong to the opposite sex or show a mixture of male and females features (Ghallioungui and Ghareeb, 1978).

Other factor is bilateral mumps orchitis which is considered the most important infection which may affect the testis in post pubertal mumps orchitis while numps before puberty does not cause orchitis, orchitis is a common complication of mumps in adult men. The onset of orchitis is usually 4-6 days after the appearance of the parotitis.

About 70% of cases, the orchitis is unilateral with some degree of atrophy of the involved testis in 50% of these cases in which there has been testicular enlargement. If the mump atrophy is bilateral, sterility will result (Abdel Fattah, 1977).

Ghallioungui and Ghareeb (1978) stated that germinal cell arrest a picture found in 22% of cases of azospermia and 20% with oligospermia, as there is arrest at the primary or secondary spermatocyte stage. Pyrexia is found to be the most important cause. Also the same authors reported that sloughing or disorderly spermatogenesis is seen in 50% of cases of oligospermia.

Some endocrine causes are also reported. As the testes perform an endocrine function, physician often think that disorders of the testis are endocrine in origin.

As to the human thyroid it is first recognizable at about 1 month after conception when the embryo is approximately 3.5-4.0 nm in length. It is also considered as one of the largest endocrine organs, weighing approximately 20 grams.

The normal thyroid is made up of two lobes joined by a thin band of tissue, the isthmus.

The thyroid is closely fixed to the anterior and lateral aspects of the trachea by loose connective tissue, the isthmus. The upper margine of which generally lies just below the cricoid cartilage,

which therefore provides a convenient landmark for locating the gland, the lobes themselves lie a long the lower half of the lateral margines of the thyroid cartilage. Formation of normal quantities of thyroid hormone ultimately depends upon the availability of adequate quantities of exogenous iodine. Normally, iodine balance is maintained from dietary sources, i.e. food and water, but iodine enters the body via dietary supplementation, diagnostic agents and medications, and as a result of the use of iodine by the food processing industry. In the body, iodide is largely confined to the extracellular fluid. It is also found however, within the red blood cell and is concentrated in the intra luminal fluids of the gastrotract, notably the saliva and gastric juice. Small amounts of iodide are lost in expired air and through the skin but its major clearance occurs via the thyroid and kidneys. Iodide removed from the plasma by the thyroid is not irreversibly lost, as the thyroid contains 8 mg of body iodine and this pool of iodine has a slow turnover by about 1% (Ingbar and Borges., 1978).

Thyroid gland contains a transport mechanism (trapping mechanism), that subserves this end and provides sufficient iodine substrate for subsequent

steps in hormone formation. Iodide enters the thyroid gland from the extracellular fluid by an active transport mechanism which is an energy requiring process dependent upon continued generation of phosphate bond energy related to the function of sodium potassium- ATP ase system (Bastomsky, 1974).

The activity of the iodide transport mechanism is influenced by a variety of physiological factors, the most important of which is the level of TSH stimulation, iodide transport is enhanced by TSH and decreased by hypophysectomy. The other major factor that influences iodide transport is an internal autoregulatory system through which the intrinsic activity of the iodide transport mechanism and its responsiveness to TSH stimulation vary inversely with the glandular content of organic iodine (Ingbar and Bonges.,1978). After its transport into or regeneration within the thyroid, iodide enters into a series of reactions that ultimately lead to synthesis of active thyroid hormone, first of which oxidation of iodide by peroxidase then iodination of tyrosol residues within thyroglobulin to yield monoiodotyrosine (MIT) and diiodotyrosine (DIT) and coupling of iodotyrosines from hormonally active iodothyronine notably T_4 and T_3.