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ANDROGENS IN THE AGING MALES

Thesis

Submitted for the partial fulfillment of The MD Degree in Andrology & STDs

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المناز المالية المنازية المناز

To My Wife

&

My Family

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Abbreviations

AIS: Androgen insensitivity syndromes.

ALT: Alanine transaminase

AR: Androgen receptor.

AST: Aspartate transamirase

17 BHSD: 17 B-hydroxysteroid dehydrogenase

BMI: Body mass index

BPH: Benign prostatic hypertrophy.

cAMP: Cyclic adenosine monophosphate

cDNA: Complementary DNA

CHD: Coronary heart disease.

DBD: DNA binding domain.

DHEA: Dehydroepiandrosterone

DHT: Dihydrotestosterone

FSH: Follicular stimulating hormone.

GTP: Guanosine triphosphate.

HDL - C: High density lipoprotein cholesterol.

Hc T: Haematocrite.

IGF-1 Insulin growth factor - 1

Kb: Kilobases.

LBD: Liganed binding domain.

LH: Lutenizing hormone.

LDL - C: Low density lipoprotein cholesterol.

Lp(a): Lipoprotein "a".

NO S: Nitric oxide synthase.

NPT: Nocturnal penile tumescence.

PADAM: Partial androgen deficiency of the aging male.

PSA: Prostate specific antigen.

P450scc Cholesterol side chain cleavage enzyme cytochrome P450.

SHBG: Sex hormone binding globulin.

SRY Sex-determining region of the Y chromosome.

StAR: Steroidogenesis activator protein.

TG: Triglycerides.

Introduction & Aim of the Work

INTRODUCTION

Androgens have many important physiological actions including effects on muscle, bone, central nervous system, prostate, bone marrow and sexual function (*Tenover*, 1992).

Testosterone is by far the most important and abundant androgen in males blood. Most (about 95%) of plasma testosterone in men is produced by the Leydig cells of the testes and released into the circulation in a pulsatile manner under stimulatory control of Luteinizing hormone. Nearly all testosterone circulates in blood bound to two proteins, albumine and sex hormone – binding globulin. Only about 1-2% of testosterone circulates totally free (Tenover, 1999)

The aging male may experience a decline in sexual function, reduction of muscle mass, aching bones and depression (Kim, 1999).

Males experience a gradual decline in fertility and gonadal function rather than an abrupt decrease, in general, an annual decline of 0.4% of total testosterone level and 1.2% of free testosterone level is seen from the fifth decade, although there is great individual variability. Not all males become hypogonadal as they age, with some remaining perfectly preserved (Qian et al., 2000).

Testosterone therapy has beneficial effects on bone density, muscle mass and strength, body composition, sense of well-being and sexual function (Tenover, 1997).

Major concerns of testosterone therapy in aging males are the risks of exacerbating cardiovascular disease and the possibility of accelerating malignant prostatic disease. So, it is wise to out-weight between the potential benefits and the possible risks of androgen therapy (Kim, 1999).

AIM OF THE WORK

The aim of this work is to clarify the biological significance of age-related decline in testosterone levels and to determine the possible risks and benefits of testosterone therapy in the aging males.