# I HORMONES IN MALE INFERTILITY

### ESSAY

Submitted in partial fulfilment for the M. Sc. Degree (Clinical Pathology)

by

HANAN ABD EL SALAM SHAWKY NADEM

UNDER SUPERVISION OF

531 67

Dr. Gihan Kamal Hassen Aly

Assistant Professor of Clinical Pathology Faculty of Medicine Ain Shams University

# Dr. Nashwa Ahmed Adel EL-Badwi

Lecturer of Clinical Pathology Faculty of Medicine Ain Shams University

1993



A. JANI

to for Lang

#### LIST OF ABBREVIATION

Ab Antibody

Ag Antigen

AMP Adenosine monophosphate

ATP Adenosine Triphosphate

CAMP Cyclic Adenosine monophosphate

CLIA Chemiluminescence Immunoassay

DHEA DiHydro EpiAndrosterone

ELISA Enzyme Linked ImmunoSorbent Assay

FSH Follicle Stimulating Hormone

GnRH Gonadotropin Releasing Hormone

HRP Horse reddish peroxidase

ICMA Immuno Chemilumino Metric Assay

IRMA Immuno Radio Metric Assay

LH Luteinizing Hormone

PIF Prolactin Inhibiting Factor

PRL Prolactin

RIA Radio Immuno Assay

SHBG Sex Hormone Binding Globulin



### Acknowledgement

I would like to express my deepest gratitude to assistant professor Dr.Gihan Kamal for her kind supervision, sincere advice, valuable guidance and continuous encouragement.

I wish to extend my sincere appreciation for the assistance comments and criticism which I received from lecturer Dr. Nashwa El-Badwi, for her untiring help, advice and guidance during this work.

I would like to express my deepest appreciation to my mother, father and husband for their help and encouragement, and I record my love to my twins (Omar, Aly) and sweet daughter (Ola).

## Contents

Introduction and Aim of work.
I- Anatomy of the male reproductive system4
II- Physiology of the male sex hormones8
* Physiologic consideration8
* Gonadotropic Hormones
* Gonadal steroids15
* Prolactin23
III- Male Reproductive disorders26
* Primary testicular failure28
* Secondary (Hypothalamic or pituitary) disease35
* Ductal obstruction37
* Hyperprolactinemia40
<pre>IV- Evaluation of the male gonadal function43</pre>
V- Methods of Assay60
* Radioimmunoassay61
* Enzyme Immunoassay68
* Chemiluminescence Immunoassay74
Summary85
References90
Arabic summary

# Introduction and Aim of the Work

### INTRODUCTION

Hormonal disorders of the male reproductive system include an assortment of problems, usually resulting from aberrant operation of the hypothalamic-pituitary-gonadal axis. These relatively common disorders often lead to infertility, and are now readily understood, diagnosed and treated, (Sairam, 1983).

Measurements of peptide and steroid hormones in serum, play a key role in both investigation and the treatment of male infertility and reproductive problems (Nanji, 1984).

Prior to development of immunoassay, the methods of assay were limited to measuring hormones by bioassays for gonadotropins and chemical methods for sex steroids. Immunoassays have essentially replaced the more time consuming and expensive bioassay (Monroe, 1984).

Immunoassay systems are often quick, easy, and sensitive, with detection limits usually within the nanogram to picogram range, (Chattoraj et al., 1986).

This adjunctive testing, involving measurements of

peptide and sex-steroid hormone concentration, allow the clinician to biochemically "dissect" the hypothalamic-pituitary-gonadal axis, and ascertain the presence as well as location of the specific defect. As such, various schemes for evaluating male reproductive disorders have been developed, and the information derived from such testing represents a critical contribution to establishing the etiology of male infertility (Griffin, 1987).

## Aim of work

To review the pivotal role of laboratory assessment of peptide and sex-steroid hormones concentrations in evaluation of male infertility and reproductive disorders.

# Anatomy of the male reproductive system

### I- Anatomy of the male reproductive system

The male reproductive system consists of two testes, that produce sperms and androgens, a penis and a system of glands, the secretions of which produce most of the components of seminal fluid, in which the sperm are conveyed. This gland system consists of two bulbourethral glands (cowper's glands), the prostate, and two seminal vesicles. Ducts through which sperm pass outside the body include the epididymis, the vas deferens, and the ejaculatory duct (Kick lighter et al., 1984).

The adult testis is a spheroid with a mean volume of 18.6 ± 4.8 ml (SD). The average length is 4.6 cm (range, 2.1-3.2 cm). The testes are located within the scrotum, which not only serves as protective envelope, but also helps to maintain the testicular temperature approximately 2°C below abdominal temperature. Three layers of membranes visceral tunica vaginalis, tunica albuginea and tunica vasculosa-comprise the testicular capsule. Extensions of the tunica albuginea into the testicle as fibrous septa result in the formation of approximately 250 pyramidal lobules each of which contains coiled seminiferous tubules. Within each testis there are almost 200 m of seminiferous tubules which produce the sperms and these structure, account for 80-90%

of the testicular mass (Fig. 1). The androgen-producing leydig cells, as well as the blood and lymphatic vessels, nerves, and fibroblasts, are interspersed between the seminiferous tubules (Amelar et al., 1977).

The seminiferous tubules in the adult average 165 um in diameter and are composed of sertoli cells and germinal cells. The sertoli cells line the basement membrane and form tight junctions with other sertoli cells. These tight junctions present the passage of proteins from the interstitial space into the lumen of the seminiferous tubules thus establishing a "blood-testis barrier".

Through extension of cytoplasmic processes, the sertolicells surround developing germ cells and provide an environment essential for germ cell differentiation. In addition, these cells have been shown to be responsible for the movement of germ cells from the base of the tubule toward the lumen and for the release of nature sperm into the lumen (Sherins et al., 1978).

These cells also actively phagocytose damaged germ cells and residual bodies, which are portions of the germ cell cytoplasm not used in the formation of spermatozoa. Finally, in response to follicle-stimulating hormone (FSH) or testosterone, the sertoli cells secrete androgen-bindings

protein, a molecule with high affinity for androgens. This substance, which enters the tubular lumen, provides a high concentrations of testosterone to the developing germinal cells during the process of spermatogenesis (Swerdloff et al., 1985).

The testis contain 2 major components, which are structurally separate and serve different functions. The leydig cells, or interstitial cells, comprise the major endocrine component, the seminiferous tubules comprise the bulk of the testis and are responsible for the production of approximately 30 millon spermatozoa per day during male reproductive life (Jubiz, 1985).

There are more than a dozen different types of germ cells, they can be classified as spermatogonia, primary spermato-cytes, secondary spermatocytes, spermatids, and spermatozoa. Spermatogenesis occurs in orderly fashion, with the spermatocytes being derived from the spermatogonia via mitotic division. Through meiotic division, the spermatids are formed, they contain a haploid number of chromosomes (23). The interval from the beginning of spermatogenesis to release of mature spermatozoa into the tubular lumen is approximately 74 days, (Berger, 1983).

Fig:1- Quoted from Ganong (1983): Male genital system. Top: The testis and epididymis are in different scales from the other parts of the reproductive system. Observe the communication between the testicular lobules. Bottom: Structural organization of the human seminiferous tubule and interstitial tissue. This figure does not show the lymphatic vessels frequently found in the connective tissue. At right: Section of human testis.

Interstitial cells

Physiology of the male sex hormones