SEX HORMONES IN FEMALE INFERTILITY

E S S A Y
Submitted For Partial Fulfilment of The
Master Degree In
Clinical Pathology

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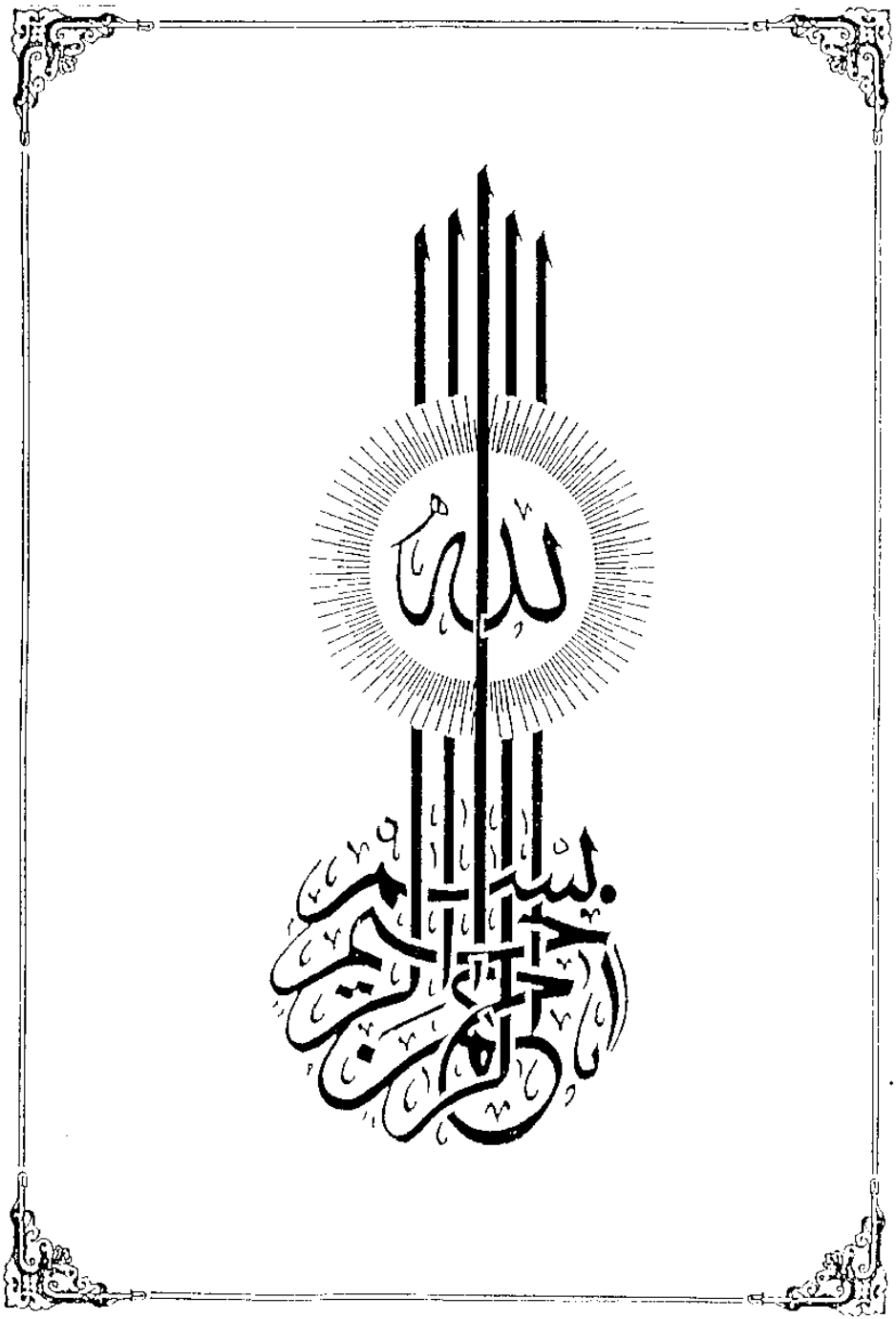
1993

ACKNOWLEDGEMENT

I wish to express my sincere gratitude to ***Dr. Gihan Kamal Hassan Aly****, Assistant Professor of Clinical Pathology, for her great encouragement, kind help, sincere guidance and supervision throughout the course of this work.*

I would also like to express my deepest gratitude to ***Dr. Farid Adly Farid****, Lecturer of Clinical Pathology. I am glad to work under his supervision,his kind care and precise instructions were of great value.*



CONTENTS

LIST OF ABBREVIATIONS

ACTH	Adrenocorticotropic hormone
ATP	Adenosine triphosphate
Δ 4	Androstenedione
CAH	Congenital adrenal hyperplasia
cAMP	Cyclic adenosine monophosphate
CBG	Corticosteroid binding globulin
CLIA	Chemiluminescence Immunoassay
CM	Cervical mucus
DHEA	Dehydroepiandrosterone
DHEA-S	Dehydroepiandrosterone sulphate
DNA	Deoxy-ribonucleic acid
E_1	Estrone
E_2	Estradiol
EIA	Enzyme immunoassay
ELISA	Enzyme linked immunosorbent assay
EMIT	Enzyme multiplied immunoassay technique
FSH	Follicle stimulating hormone
Gn RH	Gonadotropin releasing hormone
HCG	Human-chorionic gonadotropin
HRP	Horseradish peroxidase
IRMA	Immunoradiometric assay
LH	Luteinizing hormone
LHRH	Luteinizing hormone releasing hormone
LPD	Luteal-phase deficiency
mRNA	messenger ribonucleic acid
170HP	17-oH-progesterone
PCOS	Polycystic ovary syndrome
PIH	Prolactin inhibitory hormone
PRH	Prolactin releasing hormone
PRL	Prolactin
RIA	Radio immunoassay
SHBG	Sex hormone binding globulin
T	Testosterone
TSH	Thyroid stimulating hormone
VIP	Vasoactive intestinal peptide

INTRODUCTION

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Performance of the female reproductive system reflects the orderly operation of the hypothalamic-pituitary-gonadal axis. Aberrant operation of this axis can result in many different reproductive disorders, including various forms of infertility. Proper evaluation of these disorders involves a multifaceted diagnostic approach, which includes a critical contribution from the clinical laboratory. This adjunctive testing, involving the measurements of peptide and sex-steroid hormones concentrations, allows the clinician to biochemically "dissect" the hypothalamic-pituitary-gonadal axis and ascertain the presence as well as the location of the specific defect.

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 bioassays.

Immunoassay systems are often quick, easy and sensitive with detection limits usually within the nanogram to picogram range.

AIM OF THE WORK

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To review the hormonal pattern in different types of female infertility and the role of laboratory assessment of peptide and sex-steroid hormones concentrations in evaluation of female infertility and reproductive disorders.

FEMALE SEX HORMONES

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The female hormonal system consists of three different types of hormones. The first is hypothalamic releasing hormone; gonadotropin-releasing hormone (Gn RH), also called luteinizing hormone-releasing hormone (LHRH). The second type is the anterior pituitary hormones;follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Both of which are secreted in response to the releasing hormone from the hypothalamus. Another pituitary hormone is prolactin. The third type is the ovarian hormones; estrogen and progesterone which are secreted by the ovaries in response to the two hormones from the anterior pituitary *(Guyton, 1991)*.

I. GONADOTROPIN-RELEASING HORMONE

Gonadotropin releasing hormone is a decapeptide *(Rosenfield, 1990)*. Initially it was believed that there were two separate releasing hormones for follicle stimulating hormone (FSH) and luteinizing hormone (LH). It is now apparent that there is a single neurohormone (Gn RH) for both gonadotropins *(Nikolics et al., 1985)*.

Within the hypothalamus, there are neural cells which secrete the releasing and inhibiting hormones. These cells share the characteristics of both neurons and endocrine gland cells. They respond to signals in the blood stream, as well as, to neurotransmitters within the brain, in a process known as neurosecretion. In primates, the primary network of Gn RH cell bodies is located within the medial basal hypothalamus. Most of these can be seen within the arcuate nucleus where Gn RH is synthesized in GnRH neurons. The delivery of Gn RH to the portal like circulation is via an axonal pathway which is the Gn RH tuberoinfundibular tract (Fig. 1) ***(Silverman et al., 1977)***.

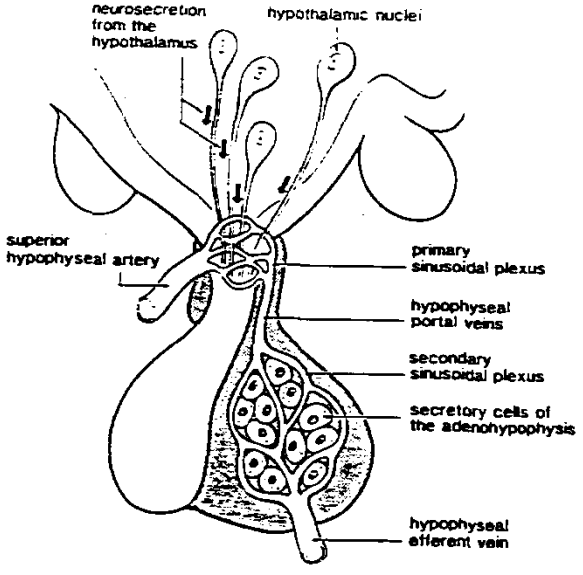

Fig. (1): Sinusoid portal system of pituitary gland

Quoted from ***(Liwnicz, 1989)***

Gonadotropin releasing hormone not only affects prompt release of preformed gonadotropins (readily releasable pool) but also stimulates the synthesis of gonadotropins (reserve pool) ***(Young and Jaffe, 1976)***. There are three principle positive actions of Gn RH on gonadotropins. The first is elaboration, synthesis and storage (the reserve pool) of gonadotropins. The second is activation and movement of gonadotropins from the reserve pool to a pool ready for direct secretion. While the third is immediate release (direct secretion) of gonadotropins ***(Veldhuis et al., 1986)***.

Normal menstrual cycle requires the maintenance of the pulsatile release of Gn RH within a critical range of frequency and amplitude. This pulsatile release is mediated by a Catecholinergic mechanism and can be modified by gonadal steroids and endorphins ***(Sameulsson et al., 1987)***.

Control of the reproductive cycle depends upon release of Gn RH, this function in turn depends upon the complex and coordinated inter-relationship among this releasing hormone, other neurohormones, the pituitary gonadotropins, and the gonadal steroids. The interplay among these substances is governed by feedback effects, both positive stimulatory and negative inhibitory (Fig. 2). The long feedback loop refers to the feedback effects of circulating levels of target

gland hormones and this occurs both in the hypothalamus and the pituitary. The short feedback loop indicates a negative feedback of gonadotropins pituitary secretion, presumably via inhibitory effects on Gn RH in the hypothalamus. Ultra-short feedback refers to inhibition by the releasing hormone on its own synthesis. These signals as well as signals from higher centers in the central nervous system may modify Gn RH secretion through an array of neurotransmitters primarily dopamine, norepinephrine, and endorphin, but also serotonin and melatonin ***(Knobil, 1980)***. Nor epinephrine is facilitatory and dopamine is inhibitory ***(Speroff et al., 1989)***. There is also evidence that endorphins are involved in the regulation of Gn RH production. The administration of naloxone, an opioid antagonist, can result in gonadotropin increase ***(Quingley et al., 1980)***.

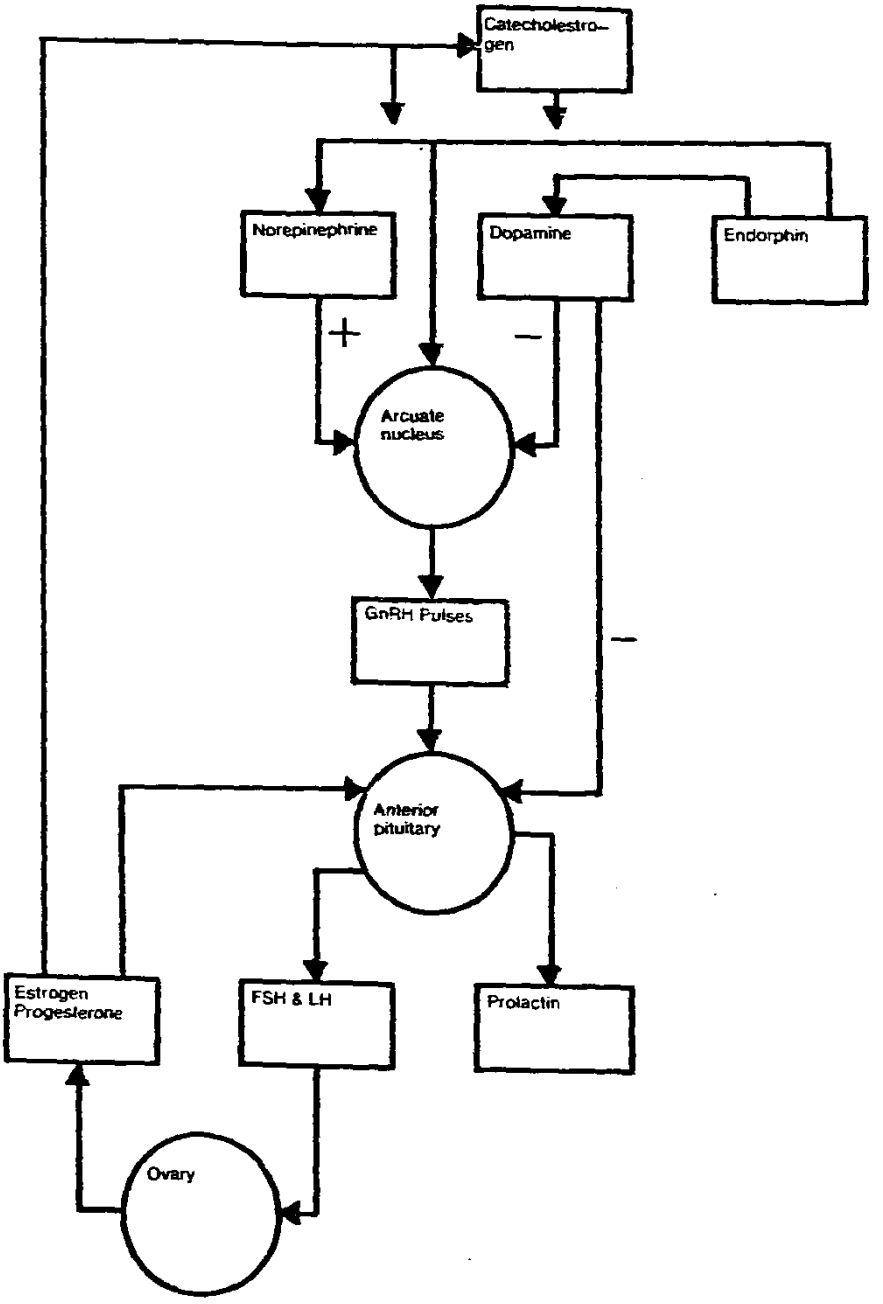

Fig. (2): Control of Gn RH pulses

Quoted from *(Speroff et al., 1989)*