GROWTH HORMONE AND INDUCTION OF OVULATION

Thesis

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M.Sc. Degree in
"Obstetrics and Gynaecology"

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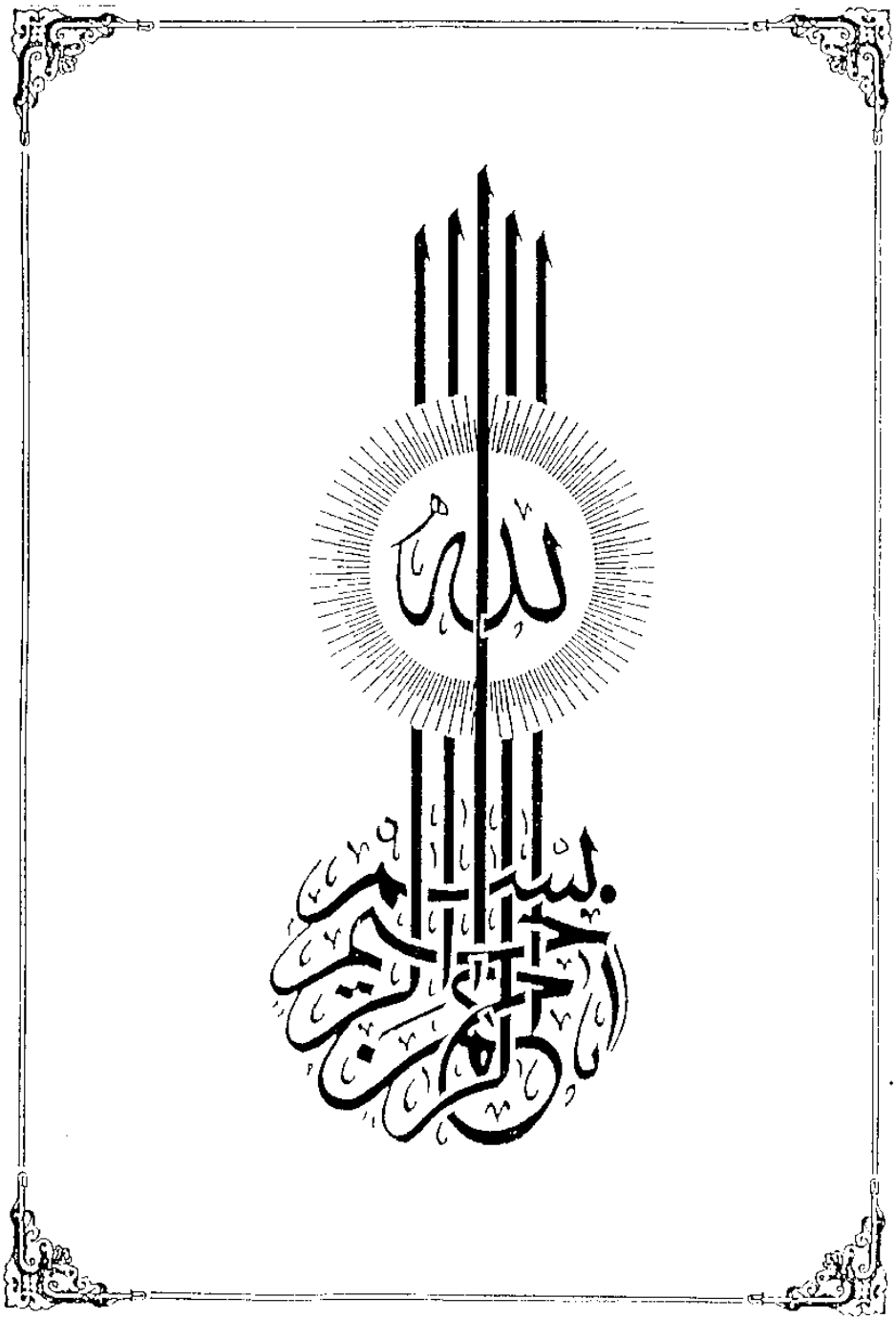


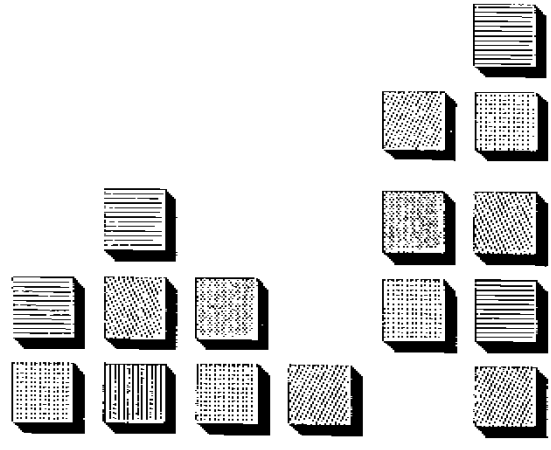
Contents

List of Abbreviations

A	Androstnendione
AVP	Arginine vasopressin
B-TGF	B-Transforming growth factor
BMI	Body mass index
CC	Clomiphene citrate
CL	Corpus luteum
CS	Chondroitin sulphate
DHT	Dihydrotesterone
E_2	Oestradiol
EGF	Epidermal growth factor
F.F.	Follicular fluid
F.G.F	Fibroblast growth factor
F.S.H	Follicle stimulating hormone
FRP	Follicle regulatory protein
GAGs	Glycosaminoglycans
GCs	Granulosa cells
GHIH	Growth hormone inhibitory hormone
GHRH	Growth hormone releasing hormone
GIFT	Gamete intrafallopian transfer
GnRH	Gonadotrophin releasing hormone
hCG	Human chorionic gonadotrophins
hGH	Human growth hormone
hMG	Human menopausal gonadotrophin
HS	Heparin sulphate

IGF-I	Insulin-like growth factor -I
IVF	In vitro fertilization
LDL	Low density lipoprotein
LH	Luteinizing hormone
LHRH	Lutenizing hormone releasing hormone
MIS	Meiosis inducing substance
MPS	Meiosis preventing substance
MSA	Multiplication stimulating activity
OCCC	Oocyte corona cumulus complex
OMI	Oocyte maturation inhibitor
P_4	Progesterone
PA	Plasminogen activators
PCO	Polycystic ovaries
PDGF	Platelet derived growth factor
PRL	Prolactin
RIA	Radioimmunoassay
SH	Somatotropic hormone
SMC	Somatomedin-c
T	Testosterone
TET	Tubal embryo transfer
VIP	Vasoactive intestinal peptide

INTRODUCTION



INTRODUCTION

Since the beginning of the recorded history the human race has placed emphasis on fertility. Nothing more vividly demonstrates the importance of fertility to the individual than the reaction by and to those who do not have children. The grief of a woman who has failed to bear a live-born child is no less in modern society than it was for our forefathers **(Lunenfeld and Insler, 1990)**.

The number of couples seeking a fertility work up is increasing every year. Approximately 10-15% of all those trying to achieve pregnancy are infertile **(Speroff et al., 1989)**. Ovulation failure is the primary defect in at least 20% of infertile couples **(Kase et al., 1990)**.

Normal ovulation requires coordination of the menstrual system at all levels: the central hypothalamic-pituitary axis, the feed back signals, and local responses within the ovary. The

loss of ovulation may be due to any one of an assortment of factors operating at each of these levels. The end result is a dysfunctional state: anovulation **(Sperof et al., 1989)**.

In the past a woman with ovulatory dysfunction had little hope of achieving a pregnancy. The successful therapy of this problem is one of the most dramatic advances in gynaecologic endocrinology. Today, if lack of ovulation is the only problem causing infertility, a persistent couple can expect their chances of conceiving to match the rate found in normal population **(Speroff et al., 1989)**.

A number of treatment possibilities are prescribed for induction of ovulation including drugs as clomiphine citrate, bromocriptine, human menopausal gonadotrophin, human chorionic gonadotrophin, cortisol derivatives or gonadotrophin releasing hormone and its analogues **(Crowely and McArthur, 1980)**. Surgical methods of induction of ovulation include wedge resection or laporoscopic cauterization of polycystic ovaries using either electrocautery or laser **(Adashi et al., 1981)**.

A possible relationship between human growth hormone (hGH) and ovarian response to gonadotrophin is recently suggested. **Homburg et al. (1988)**, demonstrated that treatment

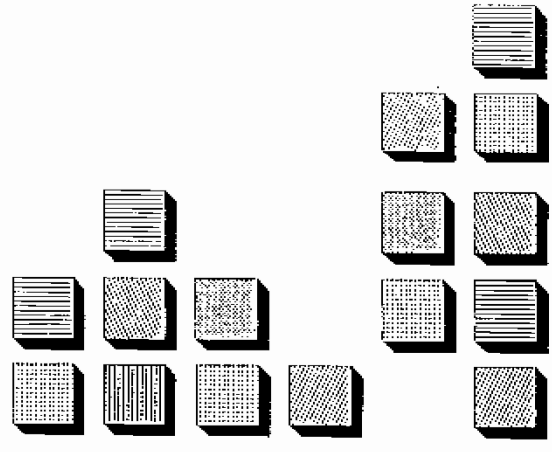
with hGH can augment the ovarian response to gonadotrophin stimulation in women with ovaries relatively resistant to human menopausal gonadotrophin therapy. These findings were confirmed by a case report by **Blumenfeld and Lunenfeld (1989)**, and by more recent trials by **Homburg et al. (1990)**; **Hugues et al. (1991)**; **Ibrahim et al. (1991)**. Yet, the findings of a recent study **(Stone and Marrs, 1991)**, challenge the speculation that endogenous pripheral hGH content relate to ovarian responsiveness to F.S.H.

Menache et al. (1990) suggested the use of clonidine as a provocative test which may help to predict responsiveness to human menophausal gonadotrophin stimulation.

During the last few year, the importance of intraovarian regulation and potentiating effect of growth hormone (GH) and various growth factors on granulosa cell response to FSH has been demonstrated **(Advis et al., 1981)**. The action of GH on the granulosa cells may be direct **(Jia et al., 1986)** or may occur via an increase in ovarian concentration or production of growth factors **(Daroven and Hsueh, 1986)**.

These findings prompted us to assess whether the level of growth hormone reserve is correlated to the ovarian response to clomiphene citrate as a method of inducing ovulation in anovulatory infertile women.

AIM OF THE WORK

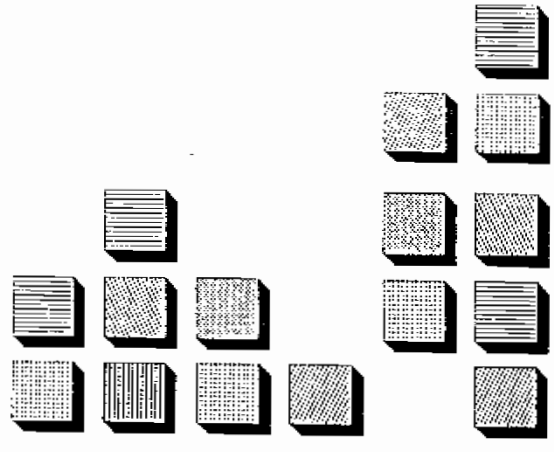


AIM OF THE WORK

The purpose of this work is:

1) To assess the clinical value of the use of clonidine (i.e. growth hormone release) as an adjuvent therapy for ovulation induction with clomiphene citrate.
2) To evaluate the possible role of growth hormone in modulation of ovarian function.

REVIEW OF LITERATURE



REVIEW OF LITERATURE

Methods of Ovualtion Induction

Ovulation is still a mysterious phenomenon: its regulatory mechanism is poorly understood and its occurrence is dfficult to detect. It is crucial for fertility and also has definite links to woman's health. A lack of or defective ovulation is one of the commonest causes of sterility in humans. Sometimes this is due to unfavourable conditions such as low body weight, excess prolaction or androgen, and once the problem has been corrected regular ovulatory cycles start again. However, the pathophysiology underlies most anovulation is still unknonw and therefore no specific treatment can be precribed for these patients. Nevertheless, the great advances in the study of ovarian physiology and the availability of powerful drugs allow an effective treatment today for the vast majority of an ovulatory women **(Crosignani, 1990)**.