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التوثيق الالكتروني والميكروفيلم



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OPTIMISING OUTCOMES IN ASSISTED REPRODUCTION (IUI, IVF, ICSI), LABORATORY AND CLINICAL ASPECTS

Thesis

Submitted for Partial Julfillment of M.D. Degree

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"Obstetrics & Gynaecology"

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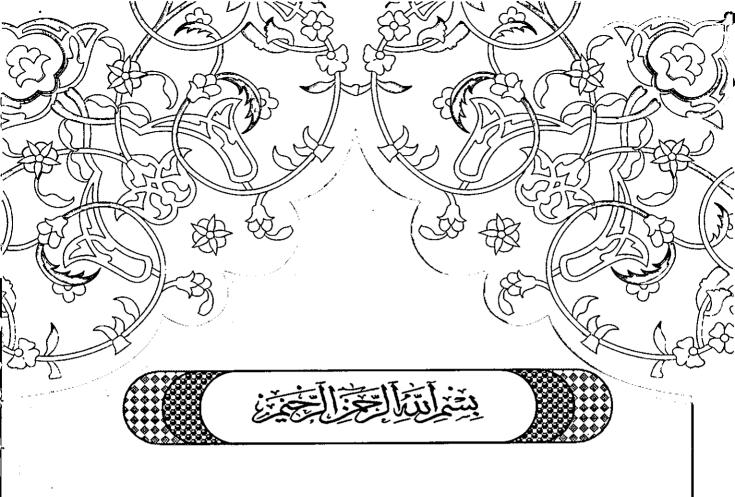
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﴿ رَبَّنَا لَا تُؤَاخِذْنَا إِن نَسينَا أَوْ أَخْطَأْنَا رَبَّنَا وَلَا تَحْمِلْ عَلَيْنَا إِصْرًا كَمَا حَمَلْنَا مَا لَا طَاقَةَ إِصْرًا كَمَا حَمَلْنَا مَا لَا طَاقَةَ لَنَا بِهِ وَاعْف عَنَا وَاغْفِرْ لَنَا وَارْحَمْنَا أَنتَ مَوْلاَنَا فَانصُرْنَا عَلَى الْقَوْمِ الْكَافِرِينَ ﴾ الْقَوْمِ الْكَافِرِينَ ﴾

صدق الله العظيم

سوره البقره (۲۸٦)

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ABREVIATIONS

AA : Amino acids

AIH : Artificial insemination husband ARTs : Assisted reproductive techniques

ATP : Adenosine tri phosphate

BBTC: Basal body temperature chart

BG: Blastocyst grade CC: Clomiphene citrate

CES : Cumulative embryo score

COH: Controlled ovarian hyperstimulation **CRH**: Corticotrophin releasing hormone

CSF : Colony stimulating factor

DES: Di ethyl stilbesterol

EGF: Epidermal growth factor

ES: Embryo score
ET: Embryo transfer

FGF : Fibroblast growth factor

FSH : Follicle stimulating hormone

G1 : Growth 1 **G2** : Growth 2

G6PDH: Glucose 6 phosphate dehydrogenase

GA: Genomic activation

GIFT: Gamete intra fallopian transfer

GLUT: Glucose transporter

GnRHa: Gonadotrophin releasing hormone analogue

GP: Glycogen phosphorelase

GPI : Glucose phosphate isomerase

HCG: Human chorionic gonadotrophin

HIV : Human immune deficiency virus

hMG: Human menopausal gonadotropin

HSPG: Heparin sulphate proteoglycan

HTF: Human tubal fluid

ICM: Inner cell mass

IGF1: Insulin like growth factor 1IGF2: Insulin like growth factor2

IL: Interleukin

Ilr : Interleukin receptor

: Intra uterine insemination IUI

: In vitro fertilisation IVF

LDH : Lacate dehydrogenase

: Lutenising hormone LH

: Leukaemia inhibitory factor LIF MAP : Mitogen activating protein MPF : M-phase promoting factor

NUMA: Nuclear mitotic apparatus protein

ODH: Oxoglutarate dehydrogrnase

OHSS: Ovarian hyperstimulation syndrome.

PAF : Platelet activating factor

PCT : Post coital test

PDGF: Platelet derived growth factor

: Pyruvate kinase PK : Placenta protein PP

PPP : Pentose phosphate pathway

PR . : Pregnancy rate PVA : Poly vinyl alcohol

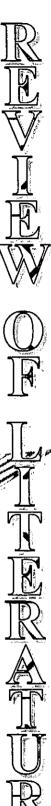
r.FSH: Recombinant follicle stimulating hormone.

RGD : Arginine-Glycine-Aspartic TCA: Tri carboxylic acid cycle TGF : Transforming growth factor

ZIFT : Zygote intra fallopian transfer

: Zona pellucida ZP







HISTORICAL REVIEW

The work of Edwards and Steptoe led to the announcement of the birth of the first human after conception in vitro, Louise Brown in July 1978. After this milestone a lot of research has been done to improve the procedure (1).

In fact the world-wide interest in IVF is to a large extent, due to enormous problem of infertility and lack of any opportunity for sterile couples to have a child of their own.

Since the milestone in 1978, human IVF has been developed and became more refined in the past few years. Further refinement of IVF has made it possible to use this technique for a variety of infertility problems. Where as in the starting days IVF was indicated for tubal pathology, now it is used for other infertility problems as endometriosis, unexplained infertility, immunologic infertility, polycystic ovary and male factor problems e.g. oligospermia (23.4).

Hormonal Stimulation:

One significant advance was the use of ovarian stimulants for successful human IVF. In the late 1960s Edwards and Steptoe tried to stimulate the growth of more than one mature follicle using hMG injection during the follicular phase of the menstrual cycle. They achieved the first human IVF pregnancy using this method but unfortunately the pregnancy turned ectopic ⁽⁵⁾.

They later abandomed the use of hMG as they believed that the hormonal environment produced by the use of hMG was abnormal and hindered implantation. Thereafter they worked on the natural cycles and they achieved the birth of Louis Brown from a natural cycle.



The first baby born after superovulation was in Australia from the group of Trounson and Wood. Nowadays almost all clinics worldwide use superovulation in their routine IVF program. Later on in 1986 GnRH agonists were introduced to reduce endogenous LH and an increase in pregnancy rate in IVF programs by the combined use of GnRH agonists and hMG has been reported ⁽⁶⁷⁾.

In addition the use of GnRH agonist has been associated with a reduction in the cancellation rates, prevention in premature LH surge and increase multifollicular growth⁽⁶⁾. More recently the predominantly FSH-containing preparations (Metrodin) was introduced in 1983. The more advanced third generation product (Metrodin HP) which is a highly purified product devoid of both LH and contaminating urinary proteins was introduced in 1993.

With more progress rFSH (recombinant FSH) was introduced in 1995 which proved to be more effective. Compared to urinary derived FSH⁽⁸⁾. Compared with urinary obtained FSH and highly purified FSH, rFSH use in women undergoing ART is associated with more embryos obtained after a lower total FSH dose administration⁽⁹⁾.

Administering hCG shortly before the expected time of spontaneous ovulation solved the problem of timing oocyte collection.

Oocyte retrieval:

Oocyte recovery is performed 34-36 hours after hCG administration⁽¹⁰⁾.

Laparoscopic oocyte recovery was the first method used for oocyte retrieval. It was developed by Steptoe who was the pioneer of laparoscopy in United Kingdom⁽¹¹⁾.



In the early eighties Scandinavian groups, particularly in Copenhagen and Gothenburg have pioneered the removal of oocytes from the follicle using ultrasound techniques⁽¹²⁾. Three different techniques have been introduced: ^(13,14).

- 1-Transvesical retrieval with an abdominal transducer
- 2-Transurethral retrieval with an abdominal transducer
- 3-Transvaginal retrieval with a vaginal transducer.

Culture technique:

Good culture technique is one of the keys to success in human IVF. Complex interactions between media components and the embryo make determination of the optimal components concentrations a difficult task. Even, in different places where good IVF results have been achieved, the composition of the media may vary. Several different culture media exist, including Earle's (15), Ham's F10 medium and Tyrode's medium(16) and CZB(17).

Culture media have gradually been developed over the past two decades.

Recently co- culturing embryos with somatic cells either in suspension or as a monolayer have alleviated inadequacies of culture media formulation⁽¹⁸⁾. The step of using co-culture in human was taken at the end of nineteen eighties⁽¹⁹⁾. Different cell types have been employed in co-culture, these included human granulocytes, human fibroblast⁽²⁰⁾, bovine tubal epithelial cells ^(21,22) and vero cells⁽¹⁹⁾. These added cells are supposed to produce substances that aid the early embryo's development such as growth factors, or alternatively remove substances that could harm it.

Co-culture is supposed to alleviate developmental block and ensure that more embryos reach the blastocyst stage.