

# A SUCCESSFUL PREGNANCY FROM THE OOCYTE DONATION PROGRAMME IN SINGAPORE GENERAL HOSPITAL

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## ABSTRACT

*A 41-year-old Chinese woman was seen in our centre in June 1989 with 5 years of premature menopause, requesting ovum donation. She was placed on cyclical hormonal therapy and put on the waiting list for ovum donation. Excess ova became available through one of our IVF patients and were fertilised with her husband's semen. Four pre-embryos resulted and these were cryopreserved using 1,2 propanediol. Embryo transfer in her second cycle of trying on 16 March 1990 of 2 pre-embryos was successful and a singleton pregnancy resulted. The pregnancy was supported with estradiol valerate and intramuscular progesterone till 17 weeks of gestation. The pregnancy went on uneventfully and she delivered a healthy baby boy by Caesarean section on 21 December 1990.*

*Keywords: premature menopause, ovum donation, cryopreservation, pre-embryos*

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## INTRODUCTION

Oocyte donation has become a reality following the report of a successful pregnancy from Lutjen<sup>(1)</sup>. Several reports of successful pregnancies have followed<sup>(2-7)</sup>.

A donor oocyte programme was set up in our Centre for Assisted Conception (CARE), Singapore General Hospital in 1989 following the establishment of a successful embryo cryopreservation programme to complement the in vitro fertilisation (IVF) programme in our centre. Donated oocytes come from patients on the IVF programme who have excess oocytes collected. The donation is anonymous and to ensure anonymity, donated oocytes are fertilized in vitro with the recipient's husband's frozen-thawed sperms and cryopreserved. Cryopreservation offers an easier method of synchronization between donor and recipient cycles for the purpose of timed embryo transfer.

## CASE REPORT

A 41-year-old Chinese woman was seen in our centre in June 1989 with 5 years of premature menopause, requesting ovum donation. She was placed on cyclical hormonal therapy, a modified regime as described by Lutjen<sup>(1)</sup> and put on the waiting list for ovum donation. Her husband's semen analysis was normal.

Cyclical hormonal therapy was as follows. Doses of up to

2 mg/day of estradiol valerate (Progynova, Schering) were given as a single morning dose, while higher doses of 6 mg/day were given as three separate 2 mg doses morning, noon and night. Intramuscular injection of progesterone (Rotexmedice GmbH) titrated according to the regime and given as one single morning dose up to 100 mg daily (Fig 1). Following the completion of the 28th day of the regimen, she immediately recommenced at day 1 of the schedule without pause and continued in this cyclic manner until embryo transfer. Endometrial dating done 5 months later on cycle day 21 showed no discrepancy. Blood progesterone levels are shown in Fig 2. It was decided to double the dosage of exogenous progesterone during the actual embryo transfer cycle as the serum levels of progesterone obtained in the prior cycle were thought to be too low.

Excess ova became available through one of our IVF patients who had consented to anonymous ovum donation and these oocytes were fertilised with her husband's semen. Four pre-embryos resulted and these were cryopreserved using 1, 2 propanediol using a modified Testart's method<sup>(8)</sup>.

Embryo transfer in her first cycle on 2 February 1990, day 17 of the artificial cycle with 2 frozen-thawed pre-embryos, (2 cell grade 1 and 4 cell grade 1 minus embryos) did not result in a pregnancy. However, the next cycle with embryo transfer on 16 March 1990 of 2 frozen-thawed pre-embryos (4 cell and 6 cell grade 1 embryos) was successful and a singleton pregnancy resulted.

Estradiol valerate was increased to 8 mg/day and intramuscular progesterone maintained at 200 mg/day after biochemical confirmation of pregnancy. The pregnancy was supported with estradiol valerate and intramuscular progesterone till 17 weeks of gestation (Fig 3). The dosages of hormones given were adjusted according to twice weekly blood levels of estradiol and progesterone. The pregnancy went on uneventfully after withdrawal of hormones and she delivered a healthy baby boy by Caesarean section on 2 December 1990.

## DISCUSSION

The success of in vitro fertilisation (IVF) has opened doors to numerous infertile couples who would otherwise have not been able to conceive on their own. Likewise, ovum donation is able to offer women with non-functioning ovaries an avenue for successful pregnancy.

In addition, this has given us an opportunity to study and understand the endocrinology of early pregnancy in the absence of ovarian function as well as uterine receptivity in the determination of successful implantation.

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Fig 1 - Estradiol valerate and progesterone cycle

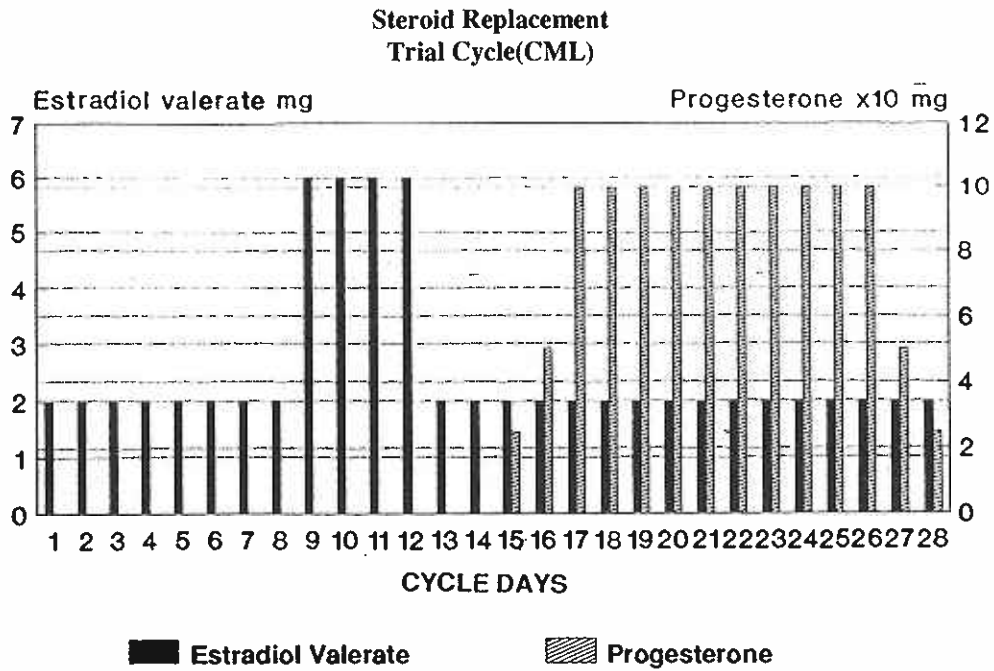
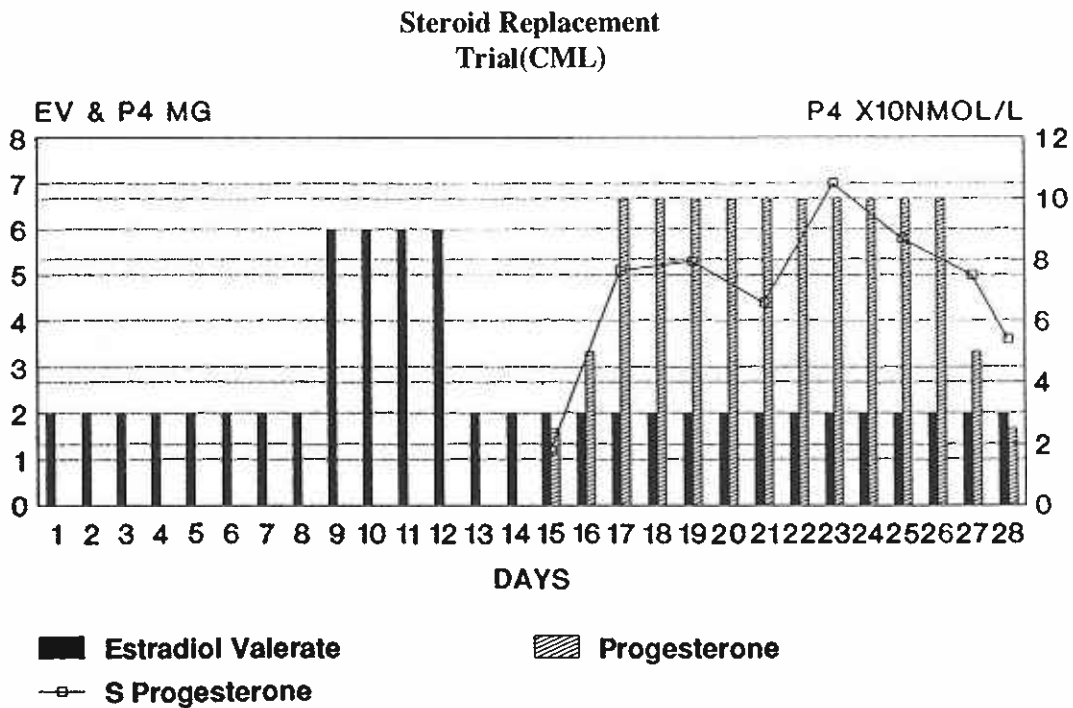


Fig 2 - Serum P4 in a replacement cycle



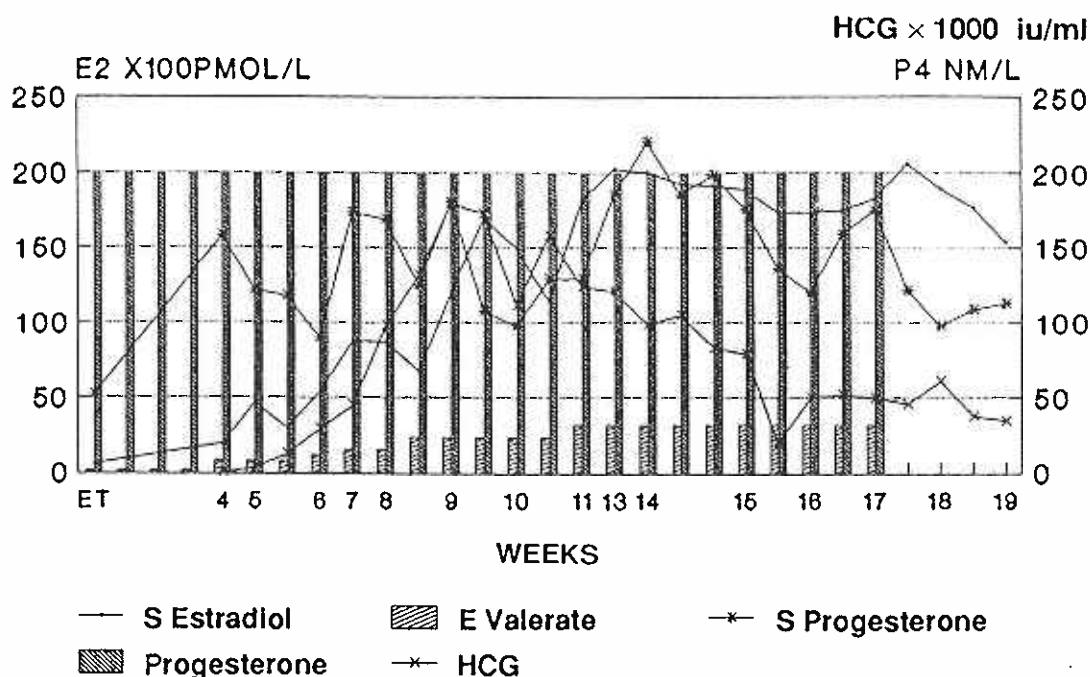
Women who have ovarian failure require steroid replacement to prime the endometrium for embryo transfer. It has been shown repeatedly that hormone substitution associated with normal endometrium resulted in successful implantation. Various combinations of sequential estrogen and progesterone regimes have been devised and used with success and this supported the concept of a large 'receptivity window' of at least 4 days in duration, pregnancies have been reported from the transfer of gametes or embryos between 1 and 4 days after the start of progesterone administration following the priming with estrogen<sup>(2,5,6,9,10)</sup>. However the ideal minimal requirements for implantation have not been fully established.

An adequate cryopreservation programme<sup>(11)</sup> has enabled us to be flexible in our ovum donation programme and maintain anonymity in ovum donation as required by the guidelines of IVF in Singapore. The success of frozen-thawed embryos resulting in pregnancies in ovum donation has been favourably reported by Salat-Baroux<sup>(10)</sup>. Following this report, Cornet<sup>(12)</sup> has reported no difference in pregnancy rates between patients receiving fresh and frozen-thawed embryos in their ovum donation programme.

The corpus luteum is an important hormonal support of early pregnancy as confirmed by Csapo and his co-workers in his findings in women who had lutectomies<sup>(13)</sup>. He has also

Fig 3 - Pregnancy levels of E2, P4 & hCG

**Steroid Replacement  
Pregnant(CML)**



confirmed the luteo-placental shift in progesterone production to be about 49 days after the last menstrual period. Theoretically, one would be able to withdraw steroids after 49 days of gestation. There have been many reports of difficulties in withdrawing exogenous progesterone at that time and withdrawal had to be delayed due to significant reduction of progesterone<sup>(1-3,5)</sup>.

In practice, we were also unable to withdraw estrogen and progesterone in this patient until 17 weeks of gestation probably erring on the side of caution. However, this does not mean that Csapo's findings were inconsistent as it has been suggested that a constant dose of steroids will mask the timing of the luteoplacental shift and a fall in estradiol and progesterone levels after steroid withdrawal may not inevitably result in miscarriage<sup>(14)</sup>.

What is baffling is the role of estrogens in early pregnancy as the level of this hormone does not appear to be

lbestrol as congenital manifestations may appear much later in life<sup>(16)</sup>.

**CONCLUSION**

The clinical applications of steroidal support of early pregnancy in agonadal women are exciting. Our centre is now using the above regime of steroid preparation of the endometrium for IVF patients who have recalcitrant ovarian function for preparation of the endometrium for frozen-thawed embryo replacement. We are also applying the knowledge obtained to support patients who have threatened abortions due to luteal defects with hormones.

Oocyte donation has a definite application in the treatment of infertility associated with ovarian failure as well as for women who have risk of inheritable disease in their offspring. They may also be applied for women who have abnormality in their oocytes and are unable to conceive otherwise.

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