THE FIRST OOCYTE DONATION PREGNANCY HOME-BRED AND DELIVERED IN SINGAPORE TO ILLUSTRATE A SIMPLIFIED OOCYTE DONATION PROGRAMME – NO MORE EMBRYO FREEZING, SYNCHRONISATION OR DISRUPTION OF SOCIAL LIFE

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ABSTRACT

The wait for an oocyte donor is highly unpredictable and stressful. The recipients may have to remain contactable at all times. Even when a donor is present, their reproductive cycles may not be in synchrony to enable gamete or embryo replacement, and embryo freezing is required for the transfer of embryos in the subsequent cycle.

After the release of the Guidelines for Assisted Reproductive Technique by the Ministry of Health[1] we have established a simplified oocyte donation programme with which the need for synchronisation, embryo freezing and the disruption to the recipient couple's social life are eliminated. To illustrate, we report the first report of oocyte donation pregnancy home bred and delivered in Singapore.

Keywords: *Oocyte donation, simplified programme, Singapore*

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INTRODUCTION

Since Lutjen[2] reported success in oocyte donation with cyclic steroid replacement therapy, many centres[3-10] in the world have reported over 100 pregnancies and 50 healthy livebirths. Though various modifications in regimes[11,12] or gamete transfer[13] have been proposed, yet the key to success is synchronisation[14] or embryo freezing[8,10] so that the gamete or embryo replacement is performed during the "window" of the recipient's cycle. The recipients' social lives are disturbed as the couples have to remain contactable anytime when donor oocytes are available for insemination.

This is the report of the first oocyte donation pregnancy home bred and delivered in Singapore using a simple and practical approach where synchronisation or embryo freezing are no longer required. With this regime all the embryos replaced are fresh and the recipients need only be contactable on 3 fixed days in every month.

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REGIME AND PROGRAMME

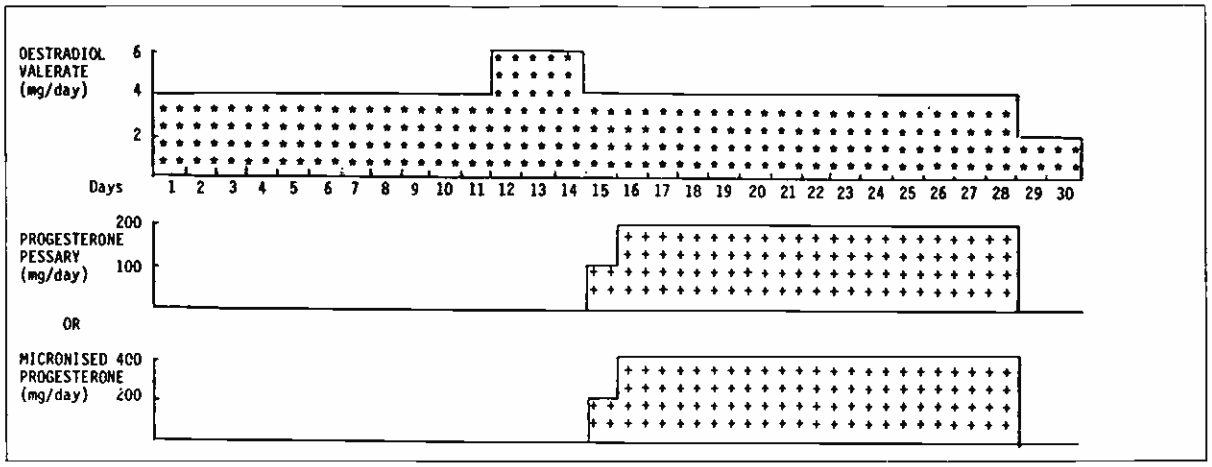
Our regime was composed essentially of progesterone replacement for 14 days using vaginal pessaries (produced by the National University Hospital Pharmacy) (10 mg at night on the first day and then 100 mg twice daily) or micronised progesterone tablets intravaginally (Utrogestan-Laboratoires Besins Iscovesco, Paris) (200 mg at night on the first day and then 200 mg twice daily)[15] . The oestrogen replacement is carried out with oral oestradiol valerate tablets (Progynova, Schering AG, Germany) 2 mg twice daily throughout the month except an increase to 2 mg thrice daily for 3 days preceding, and a decrease to 2 mg daily for 2 days following the progesterone replacement (Fig 1).

The system works best with 15 recipients or more on the waiting list. They are lined up such that individual recipient starts the progesterone replacement on 1st, 3rd, 5th...27th and 29th day of the month differently (Fig 2). If more than 15 recipients are waiting, the rest of the recipients can start the progesterone replacement on the 2nd, 4th, 6th...28th and 30th of the month. If donor oocytes will be or are available on the odd number day of the month, the recipient having the first day of the progesterone replacement on that day is identified and admitted for Gamete Intra Fallopian Transfer (GIFT) or insemination of the oocytes for subsequent embryo replacement in 2 to 3 days time. If the day happens to be the even number day of the month and no recipient is having the first day of the progesterone replacement, the recipient who is to start progesterone replacement the next day will be instructed to start the progesterone one day earlier. Thus the day of progesterone replacement becomes the same as the day of oocyte donation (Fig 2).

CASE REPORT

Madam KHH was a 36-year-old lady with premature ovarian failure when she was 26 years old. Karyotyping was normal, 46XX. Her plasma FSH was persistently over 50 iu/l and oestradiol less than 40 pg/ml. She did not receive any hormonal therapy before attending our clinic. She was married for 11 years and keen to participate in the oocyte donation programme after full counselling. She underwent an absorption test and a 28 day blood test with Cyclic Steroid Replacement Therapy (CSRT) as described by Chan et al[16] . Her plasma hormone response to oral oestradiol valerate and vaginal progesterone pessary in the 2 sets of tests were satisfactory.

Fig 1 - Cyclic Steroid Replacement Therapy Regimes



Endometrial biopsy on the 21st day of the Cyclic Steroid Replacement Therapy corresponded to day 20 to 21 as described by Noyes and Hertig[17] . Laparoscopy showed bilateral streak ovaries with both fallopian tubes suitable for gamete or embryo transfer. She was put on the oocyte donation programme as described above.

She was due to start the progesterone replacement on 21st May 1990. She was admitted for a GIFT on 20th May 1990 after 4 oocytes were donated to her. Two donor oocytes with her husband's prepared semen were transferred to each fallopian tube via laparoscopy. After the GIFT procedure, she had 100 mg progesterone pessary the same night (ie a day earlier). Afterwards, she was on oestradiol valerate 2 mg twice daily and progesterone vaginal pessaries 100 mg twice daily for 14 days until plasma hCG test confirmed the pregnancy.

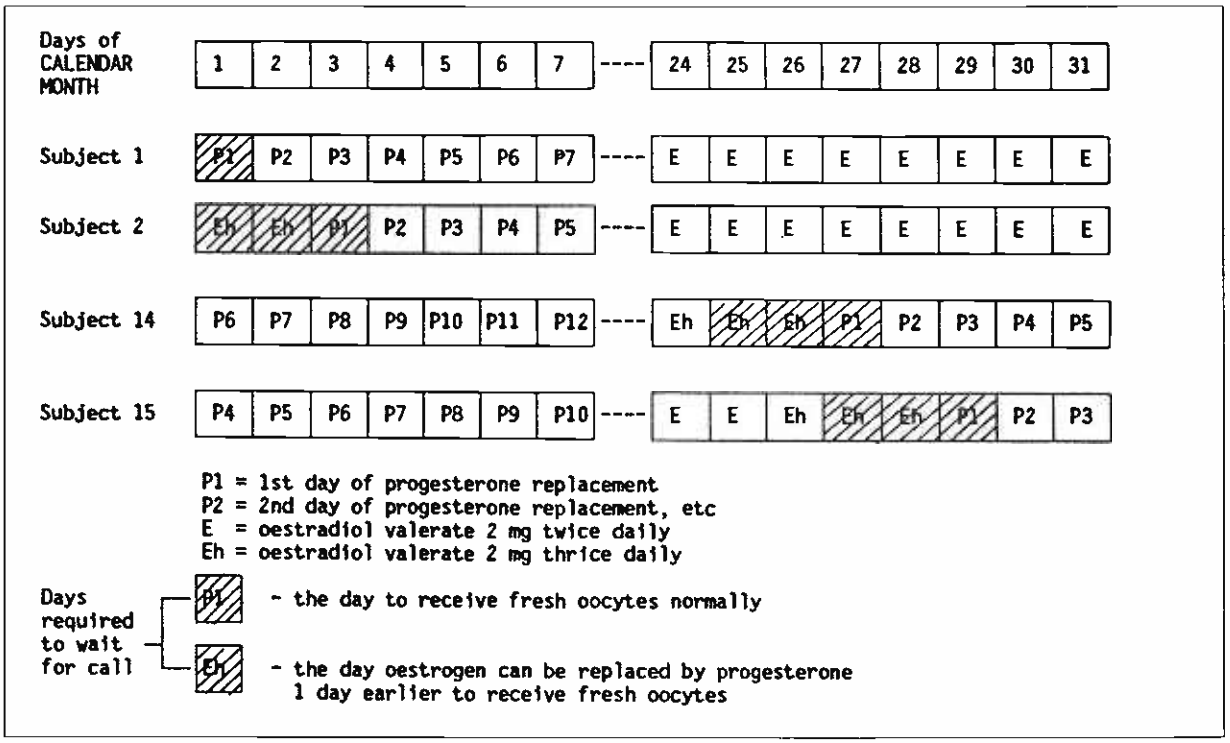
After the pregnancy was diagnosed with hCG test, the oestradiol valerate was increased to 2 mg three times daily and later to four times daily, progesterone 100 mg was administered intramuscularly daily together with the progesterone vaginal pessary 100 mg four times daily. Plasma oestradiol and progesterone levels were measured twice weekly to make sure the hormones were within the normal pregnancy range as described by Lutjen et al[18]. Transvaginal ultrasound scan at 4 weeks after GIFT confirmed a single viable intrauterine pregnancy. Starting from 11 weeks after the GIFT, the oestrogen and progesterone dosages were adjusted (ie decreased) till the luteo-placental shift had occurred. Finally oestradiol valerate was completely taken off at 13 weeks and the progesterone injection withdrawn at 15 weeks after the GIFT procedure (Fig 3 & 4). Ultrasound examination at 20 weeks showed normal singleton foetus with good growth. The antenatal course was uneventful. A healthy male baby was delivered vaginally without complications on 14th February 1991. Both the mother and the baby were discharged well the next day. Breast feeding was well established postnatally and the postnatal examination was normal.

DISCUSSION

This case report is the report of the first oocyte donation pregnancy home bred and delivered in Singapore. It opens another service of Assisted Reproductive Techniques to our Singaporean or Asian Community. It also illustrates a more organized and practical approach to our oocyte donation programme without disruption to a couple's social life.

Despite Csapo's work[19,20] that the luteo-placental shift oc-

Fig 2 - To illustrate timing and "window" to receive fresh donor oocytes



curred at late first trimester, most reports showed that pregnancies were maintained with exogenous hormones given for longer periods. Looking at Fig 3, it is appreciated that Csapo's work may be correct. The plasma E2 level never dropped on decreasing exogenous estradiol valerate 10 weeks after GIFT (ie 12 week gestation). Possibly the oestradiol valerate can be decreased much earlier. Similarly, looking at Fig 4, after progesterone was withdrawn at 15 weeks after GIFT (ie, 17 weeks gestation), the plasma progesterone ranged between 30 and 40 ng/ml, and the pregnancy went on uneventfully. As shown in Fig 4, 8 weeks after GIFT, the plasma progesterone level went

Fig 3 - Plasma oestradiol and B-hCG after G.I.F.T.

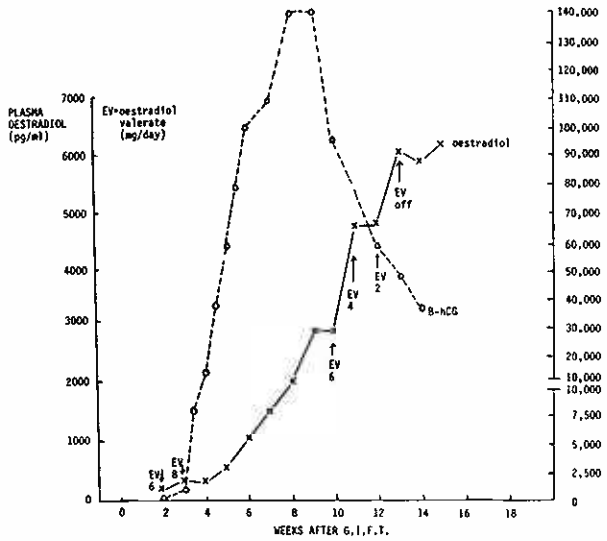
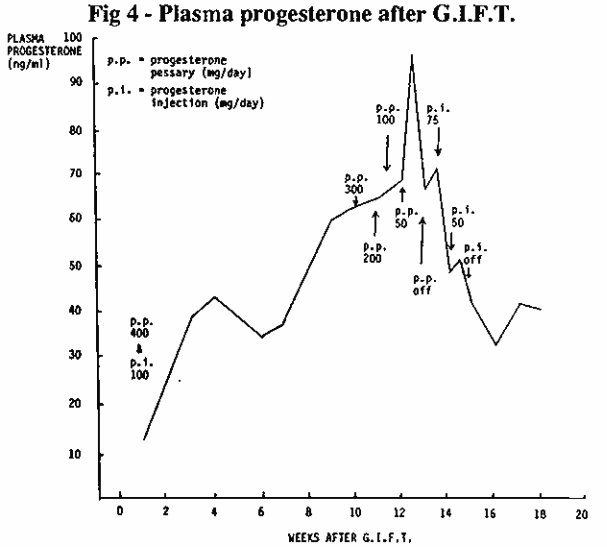


Fig 4 - Plasma progesterone after G.I.F.T.



up to 60 to 95 ng/ml with the same amount of exogenous progesterone. It was most likely that the luteo-placental shift started then. The high plasma progesterone level of 50 ng/ml or more was possibly artificially produced by the exogenous hormone and may not be essential for the maintenance of the pregnancy. It is possible a plasma level of 40 ng/ml or above may be adequate and the exogenous progesterone could have been withdrawn more quickly.

One obvious advantage of our approach is the social lifestyle of the recipient couple is not disrupted. They know exactly which 3 days they need to be contactable in any month ie from 2 days before to the day of the progesterone replacement (Fig 1).

Another advantage of this approach emerges when the number of oocytes donated are in excess of what one recipient would benefit (eg more than 4). If this happens on the odd number day of the month, the next recipient can cut short her pre-progesterone Progynova replacement by 1 or 2 days and start the progesterone replacement 1 to 2 days earlier. It is generally thought that the duration of oestrogen replacement before progesterone replacement can be variable[11-13]. Cameron et al[12] showed low dose of 2 mg oestradiol valerate daily for 10 days may be enough. Up to now, the question whether the mid-cycle oestrogen peak (which is essential for oocyte maturation) is required in this cyclic steroid replacement therapy is unanswered.

If there are excess donor oocytes on the even number days of the month, other than calling the recipient who is supposed to start the progesterone replacement the next day to start the progesterone one day earlier, the excess donor oocytes can be donated to the recipient who has started progesterone replacement the night before. Serhal and Craft[4] have reported satisfactory results with progesterone started a day prior to the retrieval of donor oocytes.

With this new approach, frozen embryo replacement is not required unless the number of oocytes donated is more than what 2 recipients could receive. There is no need for synchronisation because for every day of the month, there would be 2 recipients ready. All our patients welcome this approach as their lifestyles are less disturbed and less stressful.

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