

# **Pregnancy rates using different hormonal stimulations for frozen embryo replacement cycles**

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## **abstract**

**A total of 166 consecutive frozen embryo replacement cycles were attempted during a 10 month period in 1991. Thirty five patients had ovulation monitoring during an unstimulated cycle. LH surge was determined with a urine ovulation test kit and embryo thawing and replacement was timed so the thawing was done at the same interval after ovulation compared to the oocyte collection time (synchrony) or up to 12 hours earlier (Cohen et al, 1988). Eleven patients had a natural cycle but did not use an ovulation kit to predict the LH surge. Instead, hCG was given to allow for precise timing of ovulation and embryo thawing and replacement was calculated from synchrony as in the first 35 natural cycle replacements. Eight clinical pregnancies were established from these 46 embryo replacements (17.4% per replacement). In one hundred consecutive frozen embryo replacements accomplished during the same time period in women with a history of anovulation or irregular cycles, when follicular stimulation was necessary, clomiphene citrate (CC), hMG, or a combination of CC/hMG were administered. Another therapy used was leuprolide acetate (LA) for pituitary suppression, along with estradiol (E<sub>2</sub>) and progesterone (P) for endometrial development. Patients with no ovarian function using donated oocytes for their IVF cycle were given E<sub>2</sub> and P for endometrial development. Fourteen clinical pregnancies resulted from these 120 transfers (11.7%) per replacement.**

## **Introduction**

Cryopreservation of human embryos after IVF has become a commonly used technique to store extra embryos available after embryo replacement. Embryos are also cryopreserved in cases where ovarian failure patients receiving donated oocytes are not ready for embryo transfer at the time of their donor's egg retrieval and all resulting embryos must be frozen until the recipient is properly prepared for embryo transfer. Several methods have been used to prepare patients for frozen embryo replacement cycles. In this study the pregnancy rates were compared when the natural cycle or 1 of 5 different stimulations was used for 166 consecutive frozen embryo transfer cycles.

## Materials / Methods

In 35 ovulatory patients the LH surge was monitored with a urine test kit and embryo thawing and replacement was timed so the thawing was done at the same interval after ovulation compared to the oocyte collection time (synchrony) or up to 12 hours earlier (Cohen et al., 1988). 50 mg progesterone (P) in oil was started 2 days before the transfer to enhance endometrial development. Eleven additional ovulatory patients were given hCG instead of using the LH test kit to time ovulation. P supplementation was started the same day hCG was given.

In 120 transfers to women with anovulatory or irregular cycles, 5 methods were randomly assigned to prepare the endometrium for frozen embryo transfer. There were 13 patients given clomiphene citrate (CC), 52 were given hMG and 2 were given CC and hMG for follicular development. These 67 patients were given hCG to stimulate ovulation and P was started the same day. In addition, 13 patients were given leuprolide acetate (LA) for pituitary suppression, with estradiol ( $E_2$ ) and P support for endometrial development (Meldrum et al., 1989). Finally, 40 patients with no ovarian function used donated oocytes for their IVF cycle,  $E_2$  and P were given for endometrial development as previously described (Check et al., in press). Progesterone was given in these 120 cycles either in oil, 50mg/day or orally, 100mg progesterone capsule, 4 per day.

Embryos were frozen at the pronuclear or 2-8 cell stage using 1.5 M 1,2 propanediol and thawed in one dilution with 1.08 M sucrose (Baker et al., 1991). Pronuclear embryos were cultured overnight before transfer. 2-8 cell embryos were transferred within a few hours of thawing or allowed to cleave overnight. One to 5 embryos were usually transferred per cycle, one patient however had 6 embryos transferred. One ectopic and 21 clinical pregnancies were included in the study. Clinical pregnancy is defined as the presence of one or more intrauterine sacs confirmed by ultrasound.

Pregnancy results were compared using Chi-square analysis or Fisher's exact test for groups of 5 or less.

## Results

The average number of embryos transferred for each stimulation ranged from 3.3 to 4.1 embryos per transfer. The number of embryo replacements and the number of clinical pregnancies for each stimulation are shown in Table 1, representing 166 consecutive replacements performed during 1991. There were no significant differences in pregnancy rates for any of the stimulations or when comparing all 46 natural cycles with the 120 stimulated and down regulated cycles. However, there were no pregnancies in 15 CC stimulated cycles.

The individual categories of follicular stimulation and down regulation were retrospectively compared to determine which stimulation, if any gave a higher clinical pregnancy rate.

**Table 1 Comparison of number of replacements, number of pregnancies and pregnancy rates for 6 stimulations used for a frozen embryo replacement program.**

<u>Stimulation</u>	<u># of replacements</u>	<u># of pregnancies</u>	<u>% pregnant replacement</u>
None	46	8	17.4
CC	13	0	0
CC + hMG	2	0	0
hMG	52	8	15.4
E <sub>2</sub>	40	4	10.0
LA + estradiol	13	2	15.4

### Discussion

Although the number of patients in each study group was small and no significant differences in the pregnancy rates were found, since there were no pregnancies in the CC and CC with hMG groups we will not use CC for follicular development in the future.

The detrimental effect of CC might be related to an adverse effect on the endometrium. We do have data which supports an endometrial thickness requirement of  $\geq 10$  mm at the time of hCG in luteal phase LA-hMG stimulated IVF cycles with non-frozen embryo transfer (Check et al., 1991). There is similar data for thickness requirements prior to P administration and embryo replacement for women undergoing IVF using donated oocytes. In addition, our data support the importance of a 10mm endometrial thickness prior to P administration in frozen embryo transfers. The thinnest endometria are in the CC stimulated cycles. It would appear that the adverse effect may be related to this phenomenon.

### References

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