

## CASE REPORT

# Twin pregnancy following transmyometrial–subendometrial embryo transfer for repeated implantation failure

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**Most in-vitro fertilization (IVF) failures are due to failure of implantation. We present a case of a successful attempt at transvaginal/transmyometrial/subendometrial embryo transfer in a patient with seven previous failures in assisted conception cycles. We demonstrate achievement of a twin pregnancy, which resulted in the delivery of healthy twin girls in January 1997, following a novel technique of embryo transfer.**

*Key words:* embryo transfer/in-vitro fertilization/implantation/subendometrial embryo transfer/transmyometrial embryo transfer

### Introduction

In considering the rapid progress in the field of assisted conception, failure of implantation appears to be the main obstacle against increasing present pregnancy rates. Repeated in-vitro fertilization (IVF)–embryo transfer cycles confer both psychological and financial burdens upon the patients as well as upon the medical team and health authorities. It would seem reasonable to assume that finding a way to improve implantation rates (and, consequently, live birth rates) would be a major achievement with respect to IVF–embryo transfer treatment.

### Case report

#### *History*

The couple presented at the clinic following 3 years of primary infertility and underwent routine fertility screening followed by 3 years of treatment in the clinic. The wife had a complete infertility work-up and was found to have regular ovulating cycles, normal hysterosalpingogram, normal hormonal profile, and was negative for antiphospholipid antibodies (by Cogent Reagent Assay, single assessment). The husband demonstrated a normal semen profile according to the World Health Organization (1992) classification, normal hormonal profile and negative medical history. The cause of infertility was therefore categorized as unexplained. The couple received seven cycles of

treatment over a time period of 2.5 years, comprising of two Fallopian tube sperm perfusion cycles (Kahn *et al.*, 1992, 1993), four IVF–embryo transfer cycles, and one frozen–thaw embryo transfer cycle. Good fertilization was obtained in all IVF–embryo transfer cycles (>80% oocytes fertilized), with two to four good quality embryos transferred easily on each occasion (average >4 cells, no fragmentation, even cleavage). Cycle monitoring, stimulation, and ovum aspiration procedures were also comparable between each cycle. Prior to the fourth IVF–embryo transfer cycle the wife received a course of lymphocyte immunization (this was to reduce the chance of embryo rejection) plus a 2 week course of antibiotics (to reduce the chance of implantation failure due to chronic endometritis); however, this cycle was also unsuccessful. During subsequent discussion with the couple they desired to know if, in the new cycle, the embryos could possibly be ‘implanted’ deep within the endometrium in order to achieve a pregnancy.

#### *Transmyometrial–subendometrial embryo transfer cycle*

The literature was reviewed regarding the proposed technique and revealed one study involving intra-endometrial embryo transfer (Gastaldi *et al.*, 1993) using a modified Monash catheter (Cook, Brisbane, Australia) and a further technique of transmyometrial embryo transfer (Kato *et al.*, 1993; Sharif *et al.*, 1996) — although the latter technique utilized a specially designed catheter (Towako type; Cook), embryos were still placed into the uterine cavity albeit by passage through the myometrium. Thus, after consultation with the couple we agreed to attempt a combination of the two techniques, namely, insertion of the Towako needle and catheter transvaginally through the myometrium with deposition of the embryos into the junction between the myometrium and endometrium. The couple consented to this technique and a fifth IVF–embryo transfer cycle (sixth embryo transfer cycle) was commenced. Briefly, this consisted of gonadotrophin releasing hormone analogue (Triptorelin 3.75 mg; Decapeptyl; Ipsen, Paris, France) with daily human menopausal gonadotrophin administration (Humegon; Organon, Oss, The Netherlands) until a leading follicle size of 18 mm was attained; this was followed by 10 000 units of human chorionic gonadotrophin (Pregnyl; Serono, Rome, Italy) with scheduled ovum aspiration 36 h post-administration. The cycle was monitored by serum 17 $\beta$ -oestradiol estimation and by transvaginal ultrasound follicular tracking. A total of 17 mature oocytes (metaphase II) were collected using an ultrasound-guided transvaginal procedure.



**Figure 1.** Transvaginal ultrasound showing three endometrial lines and needle track with the needle tip at the junction of the endometrium and myometrium.

Following insemination with the husband's sperm, a total of 14 oocytes exhibited fertilization after 16 h of co-incubation. After a further 24 h, four embryos (2×8-cell, 2×6-cell) were prepared for embryo transfer. The patient was placed in the lithotomy position and the vagina cleaned with a swab dipped in sterile water. Light sedation was achieved by administration of 7.5 mg Midazolam (Dormicum; Roche, Basel, Switzerland). A 5 MHz transvaginal probe (Aloka 630, Japan) with needle guide was introduced into the posterior fornix, as the patient had a retroverted uterus. The needle puncture line was followed on the monitor as per oocyte retrieval procedure. A Towako transmyometrial transfer set was opened and the inner catheter passed to the laboratory for loading with embryos. The 18 gauge needle and stylet was introduced through the needle guide to bring the midpoint of the posterior uterine wall onto the puncture line showing the three endometrial layers. The needle was advanced through the myometrium until the junction with the endometrium, without puncture of the latter. The stylet was withdrawn and the pre-loaded transfer catheter (four embryos in a total of <math><30\ \mu\text{l}</math> media) was passed fully through the needle. After release of the embryos, the catheter was checked in the laboratory to ensure that all embryos had been transferred. Figure 1 shows positioning of the culture medium (containing four embryos) between the endometrium and the myometrium — the presence of embryos and medium can be clearly seen between the two regions, confirming the site of deposition. The patient rested for 2 h until she had recovered from sedation, after which she was discharged from the clinic and returned to her home. Luteal support was administered in the form of dydrogesterone, 10 mg orally, four times a day (Duphaston; Duphar, Weesp, The Netherlands). The patient returned to the clinic 17 days post oocyte retrieval for a urine pregnancy test (Abbot Laboratories, Diagnostics Division, Abbot Park, IL, USA). This gave a positive result and she was scheduled for ultrasound examinations 7 and 14 days later. The first ultrasound scan confirmed the presence of twin gestational sacs; the second scan confirmed the presence of

two fetal hearts. The pregnancy progressed to term with no significant problems and the patient delivered healthy twin girls vaginally.

## Discussion

The average pregnancy rate per embryo transfer is between 12 and 30% (Gastaldi *et al.*, 1993) indicating that the majority of IVF–embryo transfer failures are due to failure of implantation. Most commonly, embryos are transferred transcervically into the uterine cavity. As stated previously, two alternative techniques have recently been described. Sharif *et al.* (1996) reported on transvaginal–transmyometrial–intrauterine embryo transfer following difficult immediate mock transcervical transfer. Kato *et al.* (1993) performed the procedure to avoid the introduction of microorganisms into the uterus, to prevent the release of prostaglandins after passage of the embryo transfer catheter through the cervical canal, and to avoid difficult embryo transfer. Gastaldi *et al.* (1993) described a technique of actual implantation of embryos into the endometrium, using a modified Monash catheter (transcervical) under transabdominal ultrasound guidance, releasing the embryos at the junction of the endometrium and myometrium. The technique we describe serves all of the above purposes, namely, mechanical placement of the embryos between myometrium and endometrium, but avoiding the transcervical route. Further, the technique is performed utilizing a transvaginal transducer and needle guide (identical to the ovum aspiration set-up). Thus, the ultrasound picture is superior to the transabdominal one and the procedure is quick and simple to perform.

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