Making Family through Miracles of Assisted Reproductive Technology

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Since the birth of the first IVF baby in 1978,1 dramatic developments have occurred in in vitro fertilization (IVF). IVF was initially designed to overcome the problem of tubal infertility, but is now widely held to represent the treatment of choice for unexplained and male factor infertility, endometriosis, and ovarian dysfunction resistant to ovulation induction. In the early days of IVF, pregnancy rate was low, ranging 10%-15%. Therefore another technique, gamete intrafallopian transfer (GIFT) was developed to overcome this problem, and it was introduce in 1984.2 GIFT involves the placement of both gametes, sperm and oocytes, into the fallopian tube (the normal site of fertilization in the human) through the laparoscope. A pregnancy rate of 30% was impressive. Shortly after GIFT was introduced, it shared about 30%-70% of all assisted reproduction techniques. Later, by improvement of the quality of culture medium and embryo culture technique, the success rates for IVF and GIFT are comparable. Because GIFT required general anesthesia and a laparoscopy, most centers prefer to focus the majority of their cases on IVF to reduce the operation risk, time, and recovery. As a result, the percentage of GIFT cycles from 1995 to 2000 has declined by 90%. At the Infertility Unit, Siriraj Hospital, the first GIFT baby was born in 1990, and the first IVF baby in 1991. During the first 5 years of assisted reproductive technology (ART) services, 60% of cases were preformed by GIFT and declined gradually until 2005 when GIFT procedure was no longer performed at Siriraj Hospital.

IVF Procedure

Infertile couples who failed to conceive by conventional therapy are judged to be offered IVF treatment. The IVF procedure comprises 4 major steps, i.e., ovarian hyperstimulation, oocyte pick up, in vitro fertilization and embryo culture, and embryo transfer. Briefly, the hypothalamic-pituitary-ovarian axis of the female partner is suppressed using GnRH agonist on day 21 of the previous cycle. The ovaries are then stimulated using FSH starting on day 3 of the stimulating cycle. Follicular growth is monitored using transvaginal ultrasound starting on day 9 and the subsequent scan is scheduled depending on the initial size of the follicles. Serum estradiol measurement is added for monitoring in cases that are at risk of ovarian hyperstimulation syndrome (OHSS), e.g., cases with polycystic ovary syndrome. If more than 2 follicles with a mean diameter of ≥ 18 mm are present, human chorionic gonadotropin (hCG) 10,000 IU is administered. Oocyte retrieval is performed 34-36 h after hCG administration using vaginal ultrasound-guided follicular puncture under local anesthesia and intravenous sedation. All the follicles are aspirated and the oocytes are directly examined under stereo dissecting microscope, then kept in an incubator with 5% CO₂ at 37°C. The semen of the male partner has to be collected by masturbation on the same day. The sperm is prepared by two-layer Percoll discontinuous gradient to wash out seminal plasma, and good motile spermatozoa are used for insemination. The oocytes are inseminated 4-6 h after retrieval with 50,000-100,000 motile spermatozoa per oocyte. The oocytes were examined for fertilization 16-18 h after insemination. A maximum of 3 embryos are transferred into the uterine cavity on day 2 or day 3 after insemination, or 2 blastocysts are transferred on day 5. The surplus embryos are cryopreserved in liquid nitrogen at the temperature of -196°C. The luteal phase is usually supported by progesterone suppositories from the day of embryos replacement. Serum βhCG is measured on day 14 after insemination to determine pregnancy status. Clinical pregnancy is confirmed by the presence of gestational sac on ultrasound.

Intracytoplasmic Sperm Injection (ICSI)

Since IVF has become a well-established treatment procedure for several causes of infertility. It soon becomes obvious that certain couples with severe male factor infertility still could not conceive by conventional IVF. Extremely low sperm counts, impaired motility and poor morphology represent the main causes of failed fertilization in conventional IVF. In order to tackle this problem, intracytoplasmic sperm injection (ICSI) was established by injection of a single spermatozoon into the ooplasm of a metaphase-II oocyte, and the first delivery was reported in 1992.3 The ICSI procedure was introduced at Siriraj Hospital in 1995, and the first ICSI baby was born in 1996. During the early era of ICSI, there was
a concern that the natural selection process of fertilization is completely bypassed in patients with gross semen abnormalities, and the consequence may affect the children. A follow-up study of 1987 on children who were born after ICSI showed that the incidence of congenital malformations and chromosomal abnormalities of the ICSI children were comparable to those of IVF children.7

The introduction of ICSI has completely changed the clinical approach towards male subfertility. Moreover, the ICSI technique has an advantage for azoospermic patients who in the past had no chance to have their own genetic children. Actually, spermatogenesis is normal in patients with obstructive azoospermia, and it may be intact in some patients with non-obstructive azoospermia. ICSI using testicular sperm resulted in pregnancy almost the same as the one using ejaculated sperm. Testicular sperm can be obtained by the method of percutaneous epididymal sperm aspiration (PESA) using a 25 gauge needle attached to a 1 ml tuberculin syringe, to aspirate sperm from the caput epididymis. In cases that motile spermatozoa cannot be obtained from the epididymis, it is possible to retrieve from a testicular biopsy specimen, so-called testicular sperm extraction (TESE).

Egg Donation and Surrogacy

Not only the problems of male infertility have almost been completely solved, but also in female couples, who have neither eggs nor uterus, can be treated by ART procedures. It is technically feasible to transfer donated eggs from one woman to another. The baby would be the result of the husband’s sperm, a donated egg and the environment of the wife’s uterus. The indications for donation are absent ovaries, failed hormonal induction of ovulation, inherited genetic diseases transmitted through the female, premature ovarian failure, castrated patients (after surgical, radio- or chemo-therapy), and even post-menopausal women. The establishment of pregnancy utilizing egg donation is not adversely affected by the chronological age of the recipient, implying that the age-related decline in fertility is primarily related to the ageing of the oocyte and not to the lost of endometrial receptivity.

Surrogacy may be indicated for a woman who has had a hysterectomy or severe uterine malformation but has a functioning ovary. Couples in this situation can have their own genetic child by IVF using the wife’s oocytes and the husband’s spermatozoa. The embryos are then transferred to the uterus of a surrogate woman who would carry the pregnancy and give birth. The child would then be given to his/her genetic parents.

Summary

Assisted reproductive technology is currently used under wide range of indications and has become an acceptable tool in the treatment of subfertile couples. It has been estimated that there are more than 1.5 million IVF babies born worldwide by 2005. And IVF now reveals more and more miracles from embryogenesis. However, manipulation on gametes and embryos also raise legal, social, religious and ethical issues that should be seriously considered. Ethics should develop side by side with the advancing science and medicine.

REFERENCES