SHORT COMMUNICATIONS

SALT LAKE CITY, UTAH

Summary of the University of Utah in Vitro Fertilization Program

HISTORY

Serious efforts to establish an in vitro fertilization program at the University of Utah began late in 1981 when we contacted Professor Carl Woods in Melbourne, Australia. At his suggestion, three members of our team traveled to Melbourne and attended the International Symposium on in Vitro Fertilization in July 1982. In addition, we spent the following week with Drs. Ian Johnson and Alex Lampa at the Women’s Hospital in Melbourne. In February of 1983 three members of our team spent 2 days with Dr. Richard Marrs in Los Angeles.

Finally, in March of 1983 the first patient entered our program and completed ovulation induction, oocyte recovery, and embryo transfer.

METHODOLOGY

I. Criteria for Acceptance

Criteria for acceptance are as follows.

A. Married couples with infertility due to
   1. Irreversible abnormality of the fallopian tubes (including absence of the fallopian tubes)
   2. Semen defects
   3. Unexplained infertility
   4. Failure to conceive after appropriate therapy for
      a. Cervical diseases or factors
      b. Tubal disease
      c. Endometriosis
      d. Semen defects (failed AID or AIH)

B. The presence of a uterus and at least one ovary that can be stimulated to ovulate and from which an oocyte can be recovered at laparoscopy

C. Age and health suitable to undertake ovulation induction, laparoscopy, and pregnancy. In general, women under the age of 40 years who do not have serious systemic diseases are potential candidates.

II. Outline of the Program

A. Standard infertility tests are used to determine that a couple is suitable for the procedure, including laparoscopy to establish the accessibility of at least one ovary.

B. Frequent blood tests are taken on an around-the-clock basis in an attempt to predict the time of ovulation, and/or fertility drugs are used in an effort to produce ovulation at a predictable time.

C. Ultrasound examinations are used to assist in attempting to predict the time and number of developing eggs.

D. The wife is sometimes admitted to the hospital about 2 days before expected ovulation.

E. A sperm specimen is obtained from the husband by masturbation, and the sperm are treated in the laboratory to prepare them for fertilization.

F. The wife undergoes laparoscopy about 1–4 hr before she is expected to ovulate and a needle is inserted into the ovary in an attempt to obtain the egg(s).

G. The egg(s) and sperm are mixed together to allow fertilization to occur.

H. After fertilization, the egg is transferred into a different medium for growth.

I. After several cell divisions, if the embryo(s) appears to be developing normally, it is transferred into the wife’s uterus.

J. Blood samples are obtained after embryo transfer in an attempt to determine if pregnancy has occurred and is proceeding normally.
III. Details of the Program

A. Ovulation Induction. Ovulation induction begins with a baseline ultrasound on day 2 of the menstrual cycle. If the ultrasound demonstrates normal ovarian size, clomiphene citrate, 50–150 mg per day, is given from day 3 through day 7. Another ultrasound is performed on day 8. If the largest follicle is less than 1.4 cm in diameter, Pergonal is administered, 2 ampules per day. Serum estradiol concentrations and ultrasound examinations of ovarian size are determined every day or every other day. When two or more follicles have reached a diameter of 1.8 to 2.0 cm and the serum estradiol concentration is equal to approximately 400–450 pg times the number of follicles over 1.8 cm in diameter, 4000 units of human chorionic gonadotropins is administered if there is no evidence of a spontaneous surge of LH. Concentrations of LH are determined every 3 hr during the 12 to 36 hr preceding hCG administration.

B. Oocyte Recovery. Oocytes are obtained during laparoscopy, performed 32 to 35 hr after hCG or the beginning of an LH surge, under general anesthesia. Anesthesia is achieved by the endotracheal administration of Isoflurane, and either open (10-mm laparoscope) or closed (5-mm laparoscope) laparoscopy is performed after a pneumoperitoneum with CO₂ is achieved. A grasping forceps is placed through a suprapubic incision to secure the ovary by grasping the uteroovarian ligament. A 13-gauge, 45-cm Teflon-coated needle is then placed through a midline incision midway between the other two incisions. At a pressure of 150–200 mg Hg, oocytes are aspirated from the ovarian follicles. The follicular fluid is transferred to the embryo culture laboratory, which is adjacent to the operating room.

C. Preparation of Sperm. Semen collection occurs approximately 3 hr before the addition of the sperm to the egg. Twenty to thirty minutes after collection the sample is checked for motility, viability, and morphology. Depending on the count, 1 to 3 ml of semen is added to Ham’s F-10 incubation medium containing 8% patient’s serum at a ratio of 1 part semen to 2–3 parts medium. The solutions are mixed and centrifuged at 250g for 10 min. The supernatant is decanted and the pellet washed and centrifuged one additional time with medium. After the second wash the pellet is mixed in 0.25 ml of medium and carefully layered on top of the semen mixture. The preparation is incubated for 45–90 min and the top 1 ml of medium containing the sperm is diluted so that 40–100 µl of medium, containing approximately 400,000 motile sperm, is added to each egg. The sperm are then incubated for 1 additional hr before addition to the eggs.

D. Fertilization and Embryo Culture. Eggs are preincubated for 7 to 35 hr, depending on their maturity, before 400,000 motile sperm are added to each egg. The eggs are incubated and fertilized in modified Ham’s F-10, containing 8% patient’s serum. Fifteen hours post-sperm addition the eggs are removed, the surrounding cumulus cells are removed with needles, and the eggs are examined for evidence of fertilization. The medium is also examined for sperm motility, etc. Fertilized eggs are transferred to growth medium containing 16% serum for an additional 24 to 26 hr, at which time they are transferred in 20–100 µl of medium containing 70% patient’s serum.

E. Embryo Transfer. All embryos are placed into the uterus approximately 48 hr after oocyte recovery. They are drawn into an open-ended catheter with approximately 50 µl of transfer medium. The catheter is then placed through a hollow guide which has been placed through the internal cervical os and whose tip is approximately 1.5 cm from the fundus. The transfer catheter is advanced until its tip is approximately 0.5 cm from the fundus. The embryo(s) is then expelled from the transfer catheter into the uterine cavity. The hollow guide and transfer catheter are both removed and inspected under a dissecting microscope to ensure that the embryo(s) have been transferred. The patient remains in either modified knee–chest or supine position for approximately 4–6 hr and is then sent home.

Progesterone in oil, 100 mg, is administered daily for 3 days, beginning with oocyte recovery. Progesterone, 25-mg suppositories, is administered twice a day thereafter until a period begins or, in the absence of menses, pregnancy is ruled out by a negative serum β-hCG 3 weeks or more after embryo transfer.

Table I. Results

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<th>B</th>
<th>C</th>
<th>D</th>
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<td>C. Oocyte recovery</td>
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