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## Establishment of a Successful in Vitro Fertilization (IVF) and Gamete Intrafallopian Transfer (GIFT) Program in Malaysia

In vitro fertilization and embryo transfer (IVF-ET) and gamete intrafallopian transfer (GIFT) programs were started at the Subang Jaya Medical Centre (SJMC) in March 1986. The programs were established by PIVET Laboratory (Malaysia) and conducted by a local team of doctors and laboratory staff. During the initial stages of the program, training and supervision of both clinical and laboratory staff were conducted by senior members of PIVET Infertility Management Services at the PIVET Medical Centre in Perth, Western Australia. This summary reports the results of the initial 12 months of experience with IVF-ET and GIFT procedures in Malaysia, up to the end of March 1987.

Twenty couples had a total of 23 treatment cycles in the IVF-ET program and 42 couples had a total of 53 treatments in the GIFT program. The preliminary investigations were performed according to the protocols of the established PIVET service program (*Med J Aust* 1987;146:657-658) and included couples with tubal disorders, oligospermia, endometriosis, antispermatozoal antibodies, polycystic ovary disease (PCO), and disordered ovulatory cycles and one case of failed AID. Ovarian stimulation was generally by clomiphene citrate with or without added human menopausal gonadotropin (hMG) (Pergonal; Serono, Rome, Italy). Patients identified with high basal luteinizing hormone (LH) or PCO (*Br J Obstet Gynaecol* 1985;92:385-393) were stimulated with a combined pure follicle-stimulating hormone (FSH) (Metrodin; Serono, Rome, Italy) and hMG regimen. Cases were monitored by daily rapid hormonal radioimmunoassays from blood samples collected at 8:00 AM on the eighth day of the cycle (estradiol 17- $\beta$ , E<sub>2</sub>; progesterone, P<sub>4</sub>; and LH) and pelvic ultrasound scanning to identify follicle development. Human chorionic gonadotropin (hCG), 10,000 IU, was given as the trigger when the E<sub>2</sub> level was approximately 1500 pmol/liter/follicle >1.5 cm (average of three different transonic diameters). Patients who surged spontaneously were augmented with hCG and collected at an estimated interval of 32 to 36 hr after the onset of the LH surge. The surge onset was estimated according to the level of P<sub>4</sub> rise detected. Oocyte recovery was performed at laparoscopy using the PIVET-AN1 aspiration/flushing needle system, and oocyte recovery was 85% of the follicles entered. For IVF-ET, inseminations were performed 4 hr later with 100,000 prepared motile spermatozoa/ml. The pronuclear stage was identified at 14 to 16 hr and embryo transfer was undertaken at 44 to 48 hr when embryos were noted to be between the two-cell and the eight-cell stage of cleavage. GIFT cases were treated according to the described PIVET protocol (*Fertil Steril* 1987;in press) where a maximum of four oocytes was transferred to the fallopian tubes via Teflon catheter (Cook, Australia) and the spermatozoal numbers are adjusted according to the standard or modified protocols for oligospermics and those with antispermatozoal antibodies.

In IVF, a mean of 5.7 oocytes was recovered per case and the overall fertilization rate was 52%. A total of 51 embryos was replaced during 19 transfers (2.7 per transfer). Four clinical pregnancies were achieved following the transfer of three or four embryos. The pregnancy rate was thus 21.1% per transfer. The first pregnancy was a twin but the patient suffered a placental abruption at 24 weeks, with the intrauterine death of one of the twins. The remaining twin progressed and was delivered at 37 weeks by cesarean section. She was a normal female infant weighing 2.450 kg and was delivered along with her stillborn (fetus papyraceus) sibling.

In the GIFT program the mean number of oocytes collected was 6.7 per laparoscopy and the mean number transferred was 3.7 per GIFT treatment cycle. Fourteen pregnancies occurred (34% per transfer), with nine subsequently proceeding beyond 20 weeks of gestation. The first successful case delivered on 2 June 1987, with normal twin girls weighing 2.11 and 2.09 kg, respectively.

These documented pregnancies are the first arising from IVF and GIFT procedures performed in Malaysia. Although IVF technology as it has developed to date has a limited ability to generate pregnancies in any one treatment cycle, the system appears durable enough to allow reproducibility in a unit where medical personnel and junior scientists applying an established working protocol have undertaken a relatively short training program. It may be dependent upon quality-control procedures undertaken in the major established IVF unit such as provided at the PIVET Medical Centre in Perth, Western Australia. Culture media and all equipment which will come into contact with gametes and embryos undergo assessment using a mouse model which tests the rate of development of one-cell fertilized oocytes through to expanded blastocysts, not accepting any materials where this rate is <90%.

Having successfully completed a 12-month initiation program at the SJMC in Kuala Lumpur, Malaysia, this program is now ready to embark upon further developments which will include the introduction of transvaginal ultrasound-directed techniques of oocyte recovery, the application of different ovarian stimulation protocols for patients who have responded poorly to conventional stimulation schedules, and the introduction of PROST [pronuclear-stage tubal transfer (Lancet 1987;1:1209)] where applicable for certain subgroups of infertility such as oligospermia, antispermatozoal antibodies, repeated failures from GIFT, and ovum donation.

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### **In Vitro Fertilization (IVF) and Gamete Intrafallopian Transfer (GIFT) Program at the University of Hamburg, Federal Republic of Germany: Experiences with Two Different Stimulation Protocols**

The in vitro fertilization (IVF) program at the University of Hamburg was initiated in 1984. Our experiences up to now refer to two periods with different treatment protocols. In all women treated with IVF, tubal etiology as the cause of infertility had been established. An additional male factor was found in 47%.

In the first period of application of IVF, ovarian stimulation in most cases was induced with human menopausal gonadotropin (hMG) according to the individually adjusted treatment scheme (1). The monitoring of follicular growth consisted of daily measurement of total estrogens in 24-hr urine collections and ovarian ultrasonography. Human chorionic gonadotropin (hCG), 10,000 IU, was injected at a follicular size of 17-20 mm, and estrogens at 30-50 µg/dominant follicle. Oocyte retrieval was performed either during laparoscopy or transvaginally under sonographical control. On the day of hCG application luteinizing hormone (LH) and progesterone (P) were measured at 4-hr intervals. If an endogenous LH discharge was detected, no follicular puncture was done and the cycle was canceled.

According to this protocol 109 stimulation cycles were started. In only 66 (61%) could an oocyte retrieval be performed, since in 43 cases (39%) a spontaneous LH surge occurred. In the mean 3.8 oocytes were harvested, the fertilization rate being 52%. Following embryo transfer (ET) a pregnancy rate of 11% per ET was achieved, only 6% per started stimulation cycle.

In the second period starting from 1986 all women were pretreated by daily nasal administration of the LH-RH agonist Buserelin (Hoechst, Frankfurt a.M., 1.2 mg/day) to induce a pharmacologic hypogonadotropic state (2). When complete pituitary suppression had been proven (3), hMG stimulation was started. Endocrine monitoring and IVF technique were the same as described above. According to this treatment regimen we have performed 114 IV cycles up to now. In no case was an endogenous LH discharge during hMG application detected; each started stimulation yielded successful oocyte retrieval. Preliminary data show an increased oocyte recovery rate (5.3 oocytes) as well as fertilization rate (72% of all oocytes). The pregnancy rate was 24% per stimulation cycle and 25% per embryo transfer (4). Compared to hMG stimulation without Buserelin treatment, this is a significant improvement.