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Editorial

IN-VITRO FERTILISATION AND EMBRYO TRANSFER

The birth of Loise Joy Brown on 25th July, 1978 not only kindled a bright ray of hope in the gloomy hearts of millions of women condemned to permanent childlessness but also heralded an important scientific breakthrough. Steptoe and Edwards by their painstaking work, expending well over a decade, proved that the physiological functions of the fallopian tubes can be successfully duplicated in the laboratory. Their research and that of many others working in the field of in-vitro fertilisation (IVF) has brought to light many elusive intricacies of ovum maturation, sperm capacitation, fertilisation and preimplantation development of fertilised ovum in humans. Besides, fundamental research in this field has opened the flood gates to far greater prospects in future. In fact, future work on IVF may reveal the biological secrets of origin of choriocarcinoma, may help in the development of newer contraceptives like those directed against zona pellucida, may expose the causes of embryonic wastage and may even lead us to the secrets of evolution of human species. Such and many other future potentialities apart, today, IVF and embryo transfer (ET), in the eyes of lay public and clinicians alike, is a mode of treating certain cases of infertility previously beyond the realm of medical help.

What is it?

In essence, IVF-ET consists of recovering oocytes just prior to ovulation from follicles which are ripe but have not yet ruptured, fertilising them by sperms in the laboratory culture media and hopefully introducing them in the uterine cavity for implantation. Precepts and practices vary in the execution of every stage of this complex procedure. Should one use natural cycles or stimulated cycles? Stimulated or manipulated cycles have a distinct advantage of producing superovulation making available many oocytes and thus enhancing the chance of ultimate success. What is the ideal gas for pneumo-

peritoneum during oocyte recovery? What is the optimum interval between retrieving oocytes and exposing them to sperms? At what stage of development should the embryo be transfered to the uterus? How many embryos should be transfered at a time? Views on these and many other aspects of IVF-ET vary. So do the minute details of the precise technique of oocyte recovery, laboratory procedures and embryo transfer.

Achievements

A number of teams in many countries around the world are currently engaged in IVF-ET work. Successful births are reported from England, India, Australia, Canada and U.S.A. As of July 1982, 54 pregnancies resulting in 40 live births are on record. Twenty-one of the 40 births are reported from Australia. Four sets of twins are born by this procedure, 2 in Australia, 1 in Canada and 1 in England and at least 2 more would be born this year. The number of births is increasing rapidly, and soon it may be difficult to keep a track of each and every IVF-ET birth.

Current Status

There is no doubt that the procedure has an undisputed place in the clinical management of infertility. But inspite of spectacular achievements of the last 4 years, many more years will elapse before IVF-ET is widely available to patients desperately in need of it. The current cost of the procedure—about 2000 US dollars per cycle—is prohibitive and the centres offering this service are very few. Apart from irrepairable tubal infertility, infertility due to incorrigible oligo- or oligo-asthenospermia, or intractable antibodies against the husbands sperm in the female, or idiopathic unrecognisable causes is amenable to IVF-ET. Besides it can help eliminate pregnancies with genetic defects and sex-linked diseases by employing microbiopsy of trophoblastic cells, carrying out quantitative assays of enzyme activity in single trophoblastic cells and determining the sex of the embryo before uterine transfer. The minimum requisites for employing IVF-ET are at least one ovary that can be coaxed to ovulate and is accessible for laparoscopic ovum pick up being free from adhesions, functioning uterus and fertile semen. Given these, oocytes can be recovered in 90% and fertilisation achieved in the laboratory in 90% of these oocytes. But only 25% of the embryos transferred to the uteri accomplish live births. Thus the current success rate of IVF-ET technique is about 20%. A lot of research is being directed to improve the success of ET. The stage of development of embryo at the time of transfer, technique of ET, the state of endometrium at the time of ET and desirability and methodology of supporting implantation are areas demanding special attention in our efforts to improve the outcome of ET.

Tubal Microsurgery and IVF-ET

Tubal microsurgery for pathologically blocked tubes results in live births in 10 to 40% depending on the extent of and underlying cause of tubal damage. IVF-ET promises live births to 20% and hence is naturally reserved for failures of microsurgery. Besides in many cases IVF-ET has to be preceeded by microsurgery to liberate adherent ovaries. The poor results of microsurgery for pathologically blocked tubes stem from invisible and irrepairable damage caused by the disease to the tubal mucosa and musculature of those parts of the tubes which are nevertheless

patent. If the live birth rate after IVF-ET improves to 50% it is very likely that it will replace microsurgery for pathologically blocked tubes—tubal microsurgery will then be restricted to post-sterilisation re-canalisation where it is achieving nearly 80% live births today. At the other end, admirable attempts are being made to replace these diseased tubes by transplantation of healthy tubes from donors by microsurgical techniques. The success of this to a great measure hinges around overcoming the problem of rejection of transplanted tissues. When tubal transplantation succeeds it may make IVF-ET for tubal infertility superfluous.

Freeze-preservation of preimplantation embryos

Survival of frozen mouse embryos was reported in 1972 by Whittingham *et al* and by Wilmut. This opened the possibility of freezing and storing viable preimplantation embryos for many years—possibly for decades and perhaps for even centuries—thawing them and transfering them to a suitable uterus for implantation. In fact, this technique was allegedly used by the Calcutta team resulting in the birth of Durga on 3rd October 1978. Retriving multiple oocytes following induced superovulation, fertilising them and freeze preserving the resulting embryos would make it possible to transfer some of them in following natural cycles to achieve pregnancy and possibly years later for subsequent pregnancies too. This would eliminate the need for repeated laparoscopies which are required in most of the cases today. It would also permit delaying ET to the next cycle which may be necessary for conducting screening procedures on the trophoblastic cells to eliminate genetic abnormalities.

Ethical, moral and legal problems

Society is never prepared in advance to accept potential and new scientific discoveries and their aftermaths. It always takes its own time to comprehend, adopt, accept and assimilate the fruits of such discoveries. Today, lawyers carry on split-hair arguments regarding the legalities of IVF-ET as they affect the various persons involved in it like physicians, laboratory technicians, the couple seeking this mode of treatment, the resulting child etc., moralists debate the righteousness of IVF-ET, theologians keep condemning IVF-ET for unnatural conceptions ignoring the unnatural conceptions described in mythological and religious literatures by labelling them as supernatural ones and cynics keep on brooding over the potentialities of surrogate motherhood and possibilities of cloning. In due course, different human societies will evolve their own laws and codes of conduct, compatible with their cultural backgrounds, in relation to IVF-ET. In the meantime, suffering patients will continue to be helped undaunted by sympathetic physicians and their teams.

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