Development of Assisted Reproduction

Past, Present and Future of Technologies

Assisted reproduction is one of the scientific disciplines has evolved faster in the last years. The main reason of the success offer by ART is the association of different research areas both medical and biological. The achievements allow couples to get the right of being parents.

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Louise Brown's birth in 1978, played the conquest of a specimen of the Earth. By the first time in evolution history, an animal, a rational ape, faced with reproductive limitation was able to conceive a descendant in extracorporeal way and satisfied one of its deep instincts with his technical knowledge.

This extraordinary achievement was early followed by other incredible success: *in vitro* maturation of gametes, culture of embryos to the later stage of blastocyst, frozen and storage of human gametes and embryos, oocyte and sperm donation, and cryopreservation of ovarian and testicular tissues. Moreover, the advent of human *in vitro* fertilization (IVF) over 35 years ago has made the oocyte and preimplantation embryo uniquely accessible. This accessibility has given rise to the development of micromanipulation techniques. In fact, intracytoplasmic sperm injection (ICSI) for treatment of severe male factor infertility paved the way for the use of the micromanipulator [1].

Different Techniques

Micromanipulation techniques are now an integral part of an IVF laboratory and are now employed in the oocyte/embryo to perform assisted hatching, surgical methods to remove fragments or cytoplasm transfer. Micromanipulation has also been used in the development of nuclear transfer techniques, a potential solution for creating "younger" oocytes for women of advanced maternal age and spermatozoa for azoospermic men [2]. However, the most relevant thing is the possibility of ending the transmission of hereditary diseases (Preimplantation Genetic Diagnosis, PGD) as results of combination of polar body/blastomere biopsy and molecular biology techniques, as polymerase chain reaction (PCR), fluorescent in situ hybridization (FISH), multiple displacement amplification (MDA) and others.

PGD is a recently introduced technique in the ART, involving screening for genetic and chromosomal disorders in the embryo prior to the transfer. Although PGD was offered initially to couples at risk, the scope of PGD has also been extended to infertile couples for recurrent IVF failure, repeated spontaneous abortions, advanced maternal age and extreme male factor [3]. The application of social sex selection uses the same technology as that used in the PGD for sex-linked diseases and raised significant ethical issues. In some countries, "family balancing" is allowed. Moreover, the provision of "saviour" siblings by PGD has aroused fierce controversy. PCR protocols are used to provide an HLA type for each embryo, with the intention of matching an embryo to the sick child in the family [4]. This embryo is then transferred in the hope of establishing a pregnancy; hence, having stored cord blood stems cells and potentially bone marrow as material for treating the older sibling.

This recent applications of PGD to areas as a HLA typing and social sex selection have stoked public controversy and concern, while at the same time provoking interesting ethical debates and keeping PGD firmly in the public eye. To increase the ethical debates the availability of affected embryos followed PGD cycles has allowed the possibility, with appropriate consent, for the creation of stem cell lines [5]. These cell lines will provide an invaluable *in vitro* resource for studying the development and aetiology of the phenotype arising from these single gene defects and chromosome abnormalities.

Medical, Biological and Ethical Influence

All together, these achievements not only have medical and biological interest but represent a challenge from almost all point of view and implications in all the human matter. Today, we can say that assisted reproductive technologies (ART) have produced a dramatic change in social behaviour, allowing pregnancy in non physiological conditions e.g. post menopauses ages, choosing the baby sex for religious, social or simple private reasons, delaying the motherhood age, stopping the inherited diseases´s transmission and also opening the possibilities for other familiar status: monoparental families, lesbians couples, uterine subrogation, etc. On the other hand, ART represent an emerging and dynamic biomedical market that stretches around the globe and encompasses hundreds of thousands of people. The fertility trade is in some ways analogous to the markets for personal computers, which were initially considered luxury items but migrated to the mass market. However, the introduction of property rights, rules, and institutional policies is making the marketplace more sensitive to the social, medical, and ethical issues that are emerging from the science [6]. Owing this reasons, since his beginning, assisted reproductive technologies was furiously criticised, and was a matter of religious, political, sociological and economical concerts.

IVF, initially indicated for the treatment of fallopian tube's pathology, is now the first line therapy, and almost ever the only one, for severe male factor, severe endometriosis, idiopatic long duration sterility, immunological sterility and some ovulatory disorders, and is currently considered as the most valuable tool for the treatment of such medical conditions. Its pregnancy rates are growing step by step since his beginnings and now are hundreds of medical teems around the world giving baby home rates 50% above in many cases with low multiple order pregnancy, a common complication in all the ART involving ovarian stimulation. In fact, research is currently focusing on methods to improve IVF success rates while reducing twin and triplet pregnancies and their associated increased morbidity and mortality [1]. Screening methods to identify the most viable embryos include optimizing culture conditions for prolonged culture and selection of a high quality blastocyst for transfer. The detection of molecular markers of embryonic viability in the culture medium, like the soluble human leukocyte antigen G, is another area of investigation towards the single embryo transfer. Beside scientific or technological aspects, Quality Management System is of great importance. Staff development and monitoring of staff performance in the IVF laboratory has to be considered in the next future [7].

Finally, the use of friendly drugs regimens, the ultrasound guide ovarian pick up and the drop of financial burden are changing the patient's point of view from an experimental approach as at the 80's was seen, to an accepted, well considered and safe treatment.

References

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