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Social and ethical issues in medically assisted reproductive technologies

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Medically assisted reproductive technologies (MARTs) have proven to be a boon for the barren couple and have opened out new opportunities to study early human development extracorporeally. However, these new reproductive technologies have raised a number of novel situations never experienced by mankind before. There is a need for societal readjustments to the new norms of parenthood introduced by MARTs. There are also several delicate ethical issues associated with MARTs particularly when one can visualize the temptation to carry out experiments to understand the processes of early embryonic development in humans. These must be resolved mutually by consensus amongst scientists and practitioners of MARTs as well as the beneficiaries of such research, namely, the infertile couple.

THE concept of human beings reproducing through extracorporeal conception and the creation of 'test tube' babies lay in the realms of science fiction when Aldous Huxley wrote his famous novel *Brave New World* in the 1930s. The actual birth of the world's first test-tube baby took place some four decades later although not quite like the method described by Huxley but by fertilizing human eggs outside the body and replacing the embryo back into the mother's womb – a technique now more popularly known as *in vitro* fertilization and embryo transfer (IVF-ET). Other medically assisted reproductive technologies (MARTs) were soon to follow IVF-ET and given various acronyms (see the article by Pandiyan in this issue).

The new developments in MARTs raised hopes in the minds of several infertile couples whose barrenness could so far not be treated. Consequently, there has been great public concern and debates on the social and ethical issues concerning the new reproductive technologies, especially when a third party is also involved in the procreative act. Public debates have mostly occurred in the Western world where, as a consequence of such public concern, Governments have instituted legislative mechanisms to safeguard the interests of the infertile couple. Unfortunately in India there has been much public interest only in the lay press about the introduction of MARTs in various parts of the country. Some of the press reports are technically erroneous, factually incorrect and some have even raised great hopes in the minds of infertile couple.

All these issues need to be debated widely in our country. To initiate such a debate is beyond the scope of this article, whose aims are to highlight some of the issues as visualized by the authors who have not only been responsible for successfully introducing MARTs in the country for the first time but have been practising MARTs in the private sector for the past few years.

Social issues

Sperm and ovum donation

Therapeutic donor insemination (TDI) has been practised for over a century and a 'strange' male is the biological father of the child born out of this procedure. It has been the normal practice not to reveal the identity of the semen donor to the recipient couple so that the donor is devolved of any moral responsibility for the offspring. Furthermore, the infertile couple would not like to draw attention to the male partner's infertility and the child may need protection from the psychological confusion of multiple parentage.

There is another point of view which holds that every individual has a right to know of his or her biological parent because in times of illness, ignorance about his or her genetic constitution and family medical history of the donor may be harmful. Accidental discovery of actual parenthood can harm family interrelationships and cause distrust. Such were the views voiced at the UN Convention on the Rights of the Child in 1989. Austria and Sweden have passed legislation providing access to information identifying the donor to the child when adult. Australia, The Netherlands and the UK are not far behind.

There are a number of ovum donation programmes using non-anonymous donors. Access to information identifying the donor can raise legal questions such as, whether children arising out of gamete donation can claim inheritance rights from the donor? It is also possible that by seeking out their genetic mother such children cause an unwarranted intrusion into the donor's family life. In such an instance the husband of a married donor would have a material interest in refusing consent. To avoid such awkward incidences it would be necessary to obtain a prior consent of the husband or wife (if the donor is already married) of a prospective sperm or egg donor.

Recipients of donated gametes strongly favour anonymity and possibly a complete secrecy of the donor's identity. The wisdom for such secrecy has recently been questioned. The Warnock Report[1] recommends that secrecy surrounding semen or ovum donation should be lifted and the child be told how it was conceived but the *dramatis personae* (the donor, the recipient and the children) in this act of medically assisted reproduction should remain anonymous.

Single mothers

There have always been single mothers in Society, often not by choice. Nowadays it is not uncommon for some women to demand artificial insemination to satisfy their urge for motherhood without the 'inconvenience' of a marital relationship. Such children will be illegitimate and lack a father figure in their lives. It is a fairly universally accepted view that children are better off with two parents rather than one. Single mothers may often not have anyone else to share the burden of child-rearing and will also have to bear the entire financial burden of supporting the child. As a consequence of such responsibilities, would they have enough time for the child? Britain has recently accepted the status of unmarried motherhood and the State does provide some support for single mothers.

Pregnancies in older women[2–6]

The desire to have children is an innate human trait. Human longevity has been progressively increasing during the last few decades. Many couples are now getting married when they are in their forties. Consequently, childbearing age has also increased and older women whose fecundity is reduced or have attained menopause decide to conceive. Men have often been able to father children without an age barrier. Why should a woman be denied the chance of mothering a child when it is technologically feasible to do so even up to the age of 65 years? Medical data suggest that if cases are carefully selected there is no greater risk to maternal health or in the incidence of pregnancy-related complications in older women than in the general population. Older parents are obviously likely to die sooner than younger parents but it can be argued that a few years of a loving relationship with a child is better than none at all. Of course there may be communication problems between a mother of 60 and a child. But there are other marked advantages to the child having older parents. Unlike young couples, who must often address the difficult issues of parenting after the pregnancy has occurred, older parents have had time to make their career decisions, will have more time to spend with their children and they may have also acquired adequate financial wealth to afford bringing up the child in a good environment.

Pre-selecting the gender of the unborn child[7–10]

It is now possible to alter the XY ratios of sperm populations by a variety of methods. The initial applications of this technology are likely to be limited to the laudable goals of reducing X-linked diseases and decreasing the frequency of pregnancy terminations after prenatal diagnosis of the sex of the unborn child. The dilemma is: should sex selection be allowed for nonmedical reasons and what would be the social consequences of such sex selection? The major disapproving argument is that because there is a general desire for more boys than girls, a possible imbalance in the number of males could arise creating huge social problems. Even though this may happen temporarily, it is likely to lead to greater 'demand' for females and Nature will then again drive the population into equilibrium. In India, the cultural preference for males is for varied reasons namely – the need for an heir, to avoid the burden of dowry for female children, to ensure that there will be a male child to take care of the parents during their old age and also to perform the last funeral rites. Maharashtra was the first Indian state to ban amniocentesis for determining the sex of the foetus for nonmedical indications. There is now a national ban on such procedures. It is well known that mere legislation does not end the practice – there will always be those who will get these procedures done illicitly. What is urgently needed is an awakening of social awareness that female children are as valuable and desirable as male children.

It has been argued that prenatal sex-selection must be freely available until social consciousness is awakened as the availability of such procedures may help in limiting family size as parents would not have to bring forth additional children in order to have a child of the desired sex. Furthermore, in those families where the sex of the child is a problem for whatever reasons, a child of the wanted sex would be without a doubt a desired child and it is best that all children should be desired children. Scientific monitoring of clinics offering such procedures is needed so that the wish of the patients is not exploited by unscrupulous medical practitioners or clinics.

Parent–child relationship

Parent–child bonding is important to both parents and to developing the personality of the child. Conception involving a third party may redefine parenthood and the family structure. With the advent of MARTs, a child may in theory have as many as five parents – the egg donor, the sperm donor, the surrogate mother who bears the child and the couple which raises the child. The potential emotional ramifications can be deep and troubling. The child may be left grappling with words like 'genetic mother', 'gestational mother', 'carrying mother', 'birth mother', biological mother', 'natural mother' and at the end of it all may be left to ask 'whose child am I?' Only time will tell the reaction of children born to women of 60 to having parents who could well have been grandparents and the generation gap between them. Parents, physicians and researchers have a duty to deeply ponder on these issues before embarking on MARTs.

Ethical issues

There are a number of ethical issues arising out of the practice of MARTs. These have been extensively debated and guidelines set out in the Western world to ensure that a good measure of ethical considerations is involved in the implementation of MARTs. In India there are no guidelines and it is high time that an organized body of doctors and scientists get together to evolve guidelines to suit Indian conditions.

Quality of MART services

With the treatment for infertility being sought by more and more couples a number of infertility clinics have mushroomed all over the world including this country. The Office of Technology Assessment, USA, reported[11] that many infertility clinics in the US are yet to achieve a live birth following IVF. No such data are available for India but the same is probably true.

It is important that patients understand the realistic likelihood of the success of such procedures and have a reasonable assurance of quality care. It is necessary for the practitioners to have guidelines as to what they could and should, legally and ethically, be doing and not doing. Who then should be responsible for this? The 'Warnock Report' of the Committee of Inquiry into Human Fertilization and Embryology[1] was published in 1984 in the UK. Its recommendations included setting up of a licensing body and outlines some of its functions namely the licensing of centres, inspecting them and formulating a 'rigid code of practice'. Criminal law could be brought to bear on serious offences. This would have the desired effect of eliminating poorly run clinics and protect parents from inefficient services. The Human Fertilization and Embryology Act was passed in 1990 and the Human Fertilization Embryology Authority (HFEA) was set up in 1992 (ref. 12). The HFEA has prepared a manual including a code of practice. The American Fertility Society (AFS) also has set out 'minimum standards for IVF, GIFT and related procedures' since 1984. They have proposed guidelines on gamete donor and participant screening, physician training, clinic staffing and guidelines for embryology and andrology laboratories. Compliance with such guidelines is voluntary. The Fertility Clinic Success Rate and Certification Act has been passed by the US Congress in 1992 on the recommendation of the AFS and the Society for Assisted Reproductive Technology (SART)[13]. In 1986 the Fertility Society of Australia (FSA) set up guidelines and a code of practice for units using IVF and related reproductive technologies and in 1987 the Reproductive Technologies Accreditation Committee (RTAC) was established.

Regulation of quality control in MARTs and monitoring, safety, record keeping, inspection and licensing, and requirement of sperm donor screening are necessary in India as well. Many Indian clinics are not required to give any statistics of the outcome of their treatment. No data exist on the individual doctors and the scientists' ability to successfully perform any of the MARTs.

Human experimentation

Infertile patients have a right to know when the offered treatment is a proven medical therapy and when it amounts to an experimental trial. Furthermore, because of their often intense desire to conceive, infertile patients are vulnerable to the abuses of the researcher–subject relationship. Informed consent is a prerequisite to prevent such misdemeanors.

Embryo research

Since the advent of MARTs questions pertaining to embryo research have moved out of the realms of

philosophical debate into the moral and ethical arena. The status of the embryo remains the central issue. There is no consensus as to the point at which the embryo acquires the status of a full person to enjoy the privileges of 'Human Rights'. Most of the arguments has centred around the 'moment of fertilization' as being the stage at which full human identity is achieved. Counter-arguments emphasize the process of development, representing it as a continuum and pointing out that the potential to reach human individuality achieved after fertilization may never actually be realized. The Warnock Report[1] recommended that experimentation should not be permitted after the appearance of the 'primitive streak' (which is the first visual evidence of the development of neural tissues) on the 14th or 15th day after fertilization. Countries that do approve embryo research often stipulate that the embryos used must be those that are in excess to the number required for IVF-ET and that they should not be specifically created for research.

Embryo research can contribute to improved treatment for infertility by extending knowledge about causes and treatment for infertility and thus improve success rates of MARTs, develop and test new immunocontraceptive methods and for preimplantation diagnosis of genetic disorders in biopsied blastomeres and amplifying the DNA by the polymerase chain reaction.

Guidelines for semen donation

These guidelines are specifically aimed to protect the baby from heritable genetic disorders and the mother and child from infection. The AFS developed its first guidelines for TDI in 1980 (revised in 1986, 1988, 1990 and 1993) to enable physicians provide a safe and efficient service to infertile couples[14]. A code of practice has also been laid down in the HFEA and similar guidelines have been suggested by the British Andrology Society[15].

These guidelines involve genetic screening of the donor, screening for STD, continued surveillance of the donor to provide 'safe' samples of optimal quality. It has been suggested that the semen sample be quarantined for 180 days to rule out the presence of HIV. The number of pregnancies from each donor should be restricted to 10 in larger cities and less in smaller areas to avoid inadvertent incestuous practices in the future.

Financial compensation to gamete donors

Selling of semen, eggs or pre-embryos is considered unethical by the AFS[16] and such commercial transactions are specifically prohibited by the Warnock Report[1]. Donating eggs for money makes it uncomfortably close to a form of organ trade and leaves donors open to exploitation. Some centres have found a solution to this ethical problem by compensating the donor for the time and expenses associated with undergoing IVF treatment cycles which is directly or indirectly paid by the recipient. Some centres offer free IVF or GIFT cycle treatment as compensation for excess egg donation.

Selective foetal reduction[17]

Iatrogenic multiple pregnancies can sometimes result after MARTs as a consequence of controlled ovarian hyperstimulation. Selective termination of normal foetuses in such cases presents exceedingly difficult ethical issues similar to abortion. The basis for selecting which of the foetuses to terminate is purely technical. The most justifiable argument in favour of selective foetal reduction lies in the physician's obligation to preserve the pregnancy itself and achieve the best possible outcome in the circumstances as long as the consequences of the surgical intervention are in best interests of the patient and are acceptable to the couple.

Cloning[18]

There has been considerable public interest in the possibility of producing human clones by the repeated splitting of blastomeres and producing more than one embryo from a single zygote. All this should remain in the realms of science-fiction imagination although there is reason to believe that this would be technically feasible. As many as 10 to 12 clones have been produced in the cow.

Informed consent

The chances of success of MARTs are extremely low and therefore it is necessary that the infertile couple coming for treatment are well-counselled about the success rates and prepared for the possibility of failure rather than merely raising their hopes in the chances of success. An informed consent is necessary from the couple undergoing MART treatment. The cost of the treatment and the medical, social and possible legal implications must be explained to the couple. Besides the infertile couple, the consent of gamete donors is also essential.

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Does a period of amenorrhoea raise subsequent chances of implantation in women?

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A notable feature of the recent work on IVF has been the use of oocyte donation and hormone replacement therapy (HRT) to establish pregnancies in women. This form of treatment originated through the work of Lutjen *et al.*[1], when the first pregnancy arose through the use of a sequence therapy with oestrogens and progestagens to imitate the steroidal events of the natural menstrual cycle in combination with oocyte donation and embryo transfer. Since then, several studies have shown how this form of treatment in acyclic women, e.g. those between the ages of 30 and 50, can result in pregnancy rates far higher than in cyclic women of the same age undergoing IVF with their own oocytes[2]. The lengthy debate on the causes of this higher fertility, and especially the respective roles of egg and uterus, has not led to any clear resolution of this condition. Some workers indicated that the uterus is the primary factor leading to high rates of implantation[2, 3], whereas others insisted on the donation of oocytes from younger women as the primary factor[4]. The concepts underlying these debates have even led to some clinics recommending premenopausal women to have oocytes from donors instead of using their own oocytes to establish pregnancies, to take advantage of the higher rates of implantation supposedly gained by this approach.

This brief review gives our own concepts on the causes of high fecundity in acyclic women, and extends these concepts to the establishment of high rates of pregnancy in women who are over 50 years, or are down-regulated for several months by the use of LHRH agonists. We also propose reasons for the high fecundity of young women, and an explanation of the sharp decline in fertility of women approaching menopause.

Is the reduced fecundity in premenopausal women due to a failure of the first stage of implantation?

The onset of infertility in premenopausal women may be due to a sudden loss in their ability to implant their embryos, i.e. during the first or a very early stage of the implantation process. Moreover, a period of amenorrhoea may be beneficial for the establishment of pregnancy in these and other women. This concept emerged from the studies on acyclic/agonadal women aged between 30 and 50 years, when a detailed analysis showed how the overall incidence of clinical pregnancies and implantation rates per embryo were significantly higher in them after accepting oocyte donation and HRT therapy than in cyclic women of similar ages[2] (Tables 1 and 2). It was shown that embryo quality, as assessed morphologically, was not the cause of this difference. Such evidence implied that no benefit arose from the use of oocytes from donors aged 35 and less.

When data from all cyclic and acyclic women were analysed, it was evident that the implantation rate per embryo was much higher in acyclic women. When data from *pregnant* women only were analysed, this difference was lost, for rates of implantation were identical in pregnant women in both the cyclic and acyclic groups (Table 2). This evidence inferred that uterine capacity in