REPRODUCTIVE HEALTH CARE POLICIES AROUND THE WORLD

The Work of the Multiple Births Foundation

Incidence of twin births has been steadily increasing in all developed countries since the early 1980s (1), but that of triplets has been rising much faster still. In addition to the increase in the number of multiple births, there has been an even greater rise in the number of surviving multiple birth children, due to the considerable recent improvements in neonatal care. The increase in multiple births is due largely to the widespread use of ovulation induction and multiembryo transfer in the treatment of subfertility (2), with increasing maternal age being an additional factor.

Multiple-birth children tend to be disadvantaged from the start. They are likely to be born preterm and of low birth weight (as well as having specific complications of twinning such as the fetofetal transfusion syndrome), with consequent risk of perinatal complications, death, or long-term disability.

The perinatal mortality rate in twins is nearly five times higher than in singletons, and in triplets, it is eight times higher. The neonatal mortality rate is about seven times that of singletons (3). Parents who lose one or more babies and still have a surviving child face special problems (4). They have a constant reminder of the dead child in the surviving child—especially with monozygotic (MZ) twins. Parents of multiple infants lose what many of them see as a proud status and their bereavement is often underestimated by other people, who may imply—or even say—that they are lucky still to have one healthy baby.

The loss of babies from a higher-multiple set can be particularly difficult. After many years of infertility, a mother may suddenly have three, four, or more live babies, only to see one, two, or more of them die soon after birth or die one by one over many painful months.

A 3- to 7-fold higher incidence of cerebral palsy has been found in twins compared to singletons, and it is over 10-fold in triplets (5,6). Of course the chance of any particular multiple pregnancy producing a disabled child is much greater still (5). The care of a child with special needs always brings challenges for parents: these are increased by the difficulty of caring for other children of the same age but with very different needs (7).

Some, if only a few, quintuplets and sextuplets, as well as triplets and quadruplets, have been born healthy and apparently lived happily. But for some couples expecting higher multiples with the risks and problems outlined above, a fetal reduction will seem the least bad option. However, fetal reduction is not an easy or uncontroversial solution and carries its own risk of medical and emotional complications (8).

Either choice carries risks and sadness. Yet the case for reduction can be a strong one, and couples threatened with a high-multiple pregnancy may want at least to consider the arguments before deciding what to do. Even when the babies are healthy, difficulties may arise through having to share the attention of their mother. Triadic communication and their own intrapair relationship may also adversely affect the development of multiple-birth children, particularly their language (9,10). Depression in mothers of multiple births is more common (11), as are behavioral problems among the siblings (12).

Few parents expecting twins or triplets will have any knowledge of what is involved in the care and upbringing of multiple-birth children. Failure by some professionals to recognize the problems and stresses may result in unnecessary risks being run by some infertility specialists. They are understandably keen to maximize the chance of a pregnancy,

but many couples later complain that they were never told of the possible implications of a multiple pregnancy (13). At the Multiple Births Foundation (MBF) clinics, parents of triplets often complain about this, even when the babies are healthy. In the United Kingdom, assisted conception clinics providing IVF services must be licensed by the Human Fertilisation and Embryology Authority (HFEA). The *Code of Practice* (14) by which they must abide specifically requires information on the risks and implications of a multiple pregnancy to be given before treatment is commenced.

For a childless couple the practical and emotional difficulties of caring for two or more babies at the same time may be particularly difficult to imagine. It has been shown that parents do not have realistic expectations of how the birth of twins will affect their family (15). A survey by the British Fertility Society and CHILd, a U.K. patient support group, found that 66% of respondents felt that twins would be an ideal outcome of IVF treatment (16). Mothers are often unrealistically optimistic about the likely outcome. Many are unprepared for the impact the birth of twins can have on the relationship with their partner. The father may be surprised by how much his help is needed with the baby care and may not understand how much the mother's emotions will be focused on the children. A preliminary study of families with twins after IVF indicated that parenting may be considerably less rewarding than parents had expected (17).

With practical help and early intervention from professionals, many of the longer-term problems can be avoided, but many professional carers are still not sufficiently aware of the practical, emotional, and financial stresses experienced by these families and of the special help they need.

The MBF was established in 1998 as the first organization to offer professional support to families with twins, triplets, and more, as well as information, advice, and training to the many medical, educational, and social work staff concerned with their care.

Initially the work focused largely on helping families, through Twins Clinics, parent evening meetings and literature. The Twins Clinics, run at three centers, concentrate on problems that are caused or increased by twinship such as extreme rivalry, difficulties over identity, language delay, and behavior problems in the older sibling. They also help to resolve uncertainty over zygosity. Higher-order birth families have their own 3-monthly clinic, the Supertwins Clinic, which also provides a lunchtime

gathering for the whole family. At all the clinics mutual support and reliable childcare are provided by a rota of volunteers, who are all parents of multiples themselves.

Many parents who either cannot or do not need to come to the clinics can get help from the MBF's literature, the Telephone Advisory Service, or the evening meetings. The latter focus on particular topics such as prenatal preparation, language, behavior, individuality, and schooling. An illustrated talk is followed by a panel discussion.

The Telephone Advisory Service provides booked consultations at which information, advice, and support are given to parents and adult twins, including those who have been bereaved, as well as to professionals.

One charitable organization can never itself meet the needs of all families. It is much more appropriate for the family's own professional caregivers to advise locally. The MBF is therefore now concentrating increasingly on the education of professionals. It does this through a teaching program and by sharing the services described, including the Telephone Service, as models for others to follow. There is now a wide range of written and audiovisual materials and of seminars and lectures. There is also a resource center in London.

Future plans include working closely with midwives and health visitors (community nurses) to develop models of good practice which will be disseminated nationally and internationally, with the MBF acting as a specialist information and advice center.

A series of guidelines (18) for the professional caregivers is currently being prepared for the care of multiple-birth families from before conception through adolescence. The first four of these are already available from the MBF. A summary for those working with couples at fertility clinics and maternity units is given below.

To Couples Considering Treatment for Infertility. Referring to the RCOG guidelines (19), give detailed information on the chances of a multiple pregnancy and on the consequent risks and implications to the children and the family (20). Fetal reduction should be discussed with those whose treatment could result in the conception of triplets or higher-order births.

During the Pregnancy. Provide written information including contact with local and national organizations for families with multiple births (21). In monochorionic pregnancies ensure that parents understand the implications and need for close

monitoring. Explain that a dichorionic placenta does NOT necessarily indicate dizygosity. Regarding prenatal screening, ensure that parents understand the options available if an anomaly is present in only one fetus, including selective fetocide. Provide special prenatal classes, in collaboration with local parents of twins group, for parents (and grandparents) to include guidance on feeding, equipment, sources of information and practical help, promotion of individuality and language, and the needs of older siblings. Ensure that the unit has a special protocol if a multiple-birth baby dies, as well as literature (21) and contact with a bereaved parent of twins who can offer immediate support.

REFERENCES

1. Imaizumi Y: Trends of twinning rates in ten countries, 1972–1996. *Acta Genet Med Gemellol* 1997;46:209–218
2. Loos R, Derom C, Vlietinck R, Derom R: The East Flanders Prospective Twin Survey (Belgium): A population-based register. *Twin Res* 1998;1:167–175
3. Office of National Statistics: DH3 No 29, 1997
4. Bryan EM: Perinatal bereavement after the loss of a twin. *In* Multiple Pregnancy, RH Ward, M Whittle (eds). London, RCOG Press, 1995, pp 186–195
5. Petterson B, Stanley F, Henderson D: Cerebral palsy in multiple births in Western Australia. *Am J Med Genet* 1990;37:346–351
6. Williams K, Hennessy E, Alberman E: Cerebral palsy: Effects of twinning, birthweight and gestational age. *Arch Dis Child* 1996;75:F178–F182
7. Bryan E: The disabled twin. *In* Twins and Higher Multiple Births. A Guide to Their Nature and Nurture. Sevenoaks, Edward Arnold, 1992, pp 165–170
8. Bryan E, Higgins R: Embryo Reduction of a Multiple Pregnancy: An insoluble dilemma? *In* Infertility. New Choices. New Dilemmas, E Bryan, R Higgins (eds). London, Penguin, 1995, pp 130–140
9. Mittler P: Language development in young twins: Biological genetic and social aspects. *Acta Genet Med Gemellol* 1976;25:359–365
10. Hay DA, Prior M, Collett S, Williams M: Speech and language development in preschool twins. *Acta Genet Med Gemellol* 1987;36:213–222
11. Thorpe K, Golding J, MacGillivray I, Greenwood R: Comparison of prevalence of depression in mothers of twins and mothers of singletons. *Br Med J* 1991;302:875–878
12. Hay DA, McIndoe R, O'Brien PJ: The older sibling of twins. *Aust J Early Child* 1988;13:25–28
13. Botting BJ, Macfarlane AJ, Price FV (eds): Three Four and More. A Study of Triplets and Higher Order Births. London, HMSO, 1990
14. The Human Fertilisation and Embryology Authority: Code of Practice. London, HFEA, 1998, Part 4
15. Hay DA, Gleeson C, Davies C, *et al*: What information should the multiple birth family receive before, during and after the birth? *Acta Genet Med Gemellol* 1990;39:259–269
16. Murdoch AP: How many embryos should be transferred? *Hum Reprod* 1998;13:2666–2669
17. Cook R, Bradley S, Golombok S: A preliminary study of parental stress and child behaviour in families with twins conceived by in-vitro fertilisation. *Hum Reprod* 1998;13:3244–3246
18. Bryan E, Denton J, Hallett F: Guidelines for Professionals: Multiple Births and Their Impact on Families. London, MBF. Facts About Multiple Births (1997); Multiple Pregnancy (1997); Bereavement (1997); The Twin with Special Needs (1999); The First Five Years (in press).
19. Royal College of Obstetricians and Gynaecologists: The Management of Infertility in Secondary Care. London, RCOG Press, 1998
20. Denton J: Multiple Pregnancy and Birth—For Patients Considering Treatment for Infertility. London, MBF, 1997
21. Relevant booklet for parents available from the MBF

**Elizabeth Bryan
Jane Denton**

The Multiple Births Foundation
Queen Charlotte's and Chelsea Hospital Goldhawk Road
London W6 OXG, England
e-mail: mbf@rpms.ac.uk

Legislation and Regulations Regarding the Practice of Assisted Reproduction in India

INTRODUCTION

In India, until now there has been no statutory act (legislation) or specific guidelines relating to the practice of ART. The ethics are governed by customary social practices within the community, conventional human rights, and sometimes religious

law, which is based on spiritual values. The extent of human rights is acceptable in Indian law provided the procedures of the investigations and their consequences do not harm anybody or contradict the customary practices and do not exceed the limits of popular tolerance.

Social and customary practices in India are domi-

nated mostly by religious instincts. Religionwise the Indian population can be grouped into three categories: Hindus (including Sikhs, Jains, and Parsees; 79%), Muslims (13%), and Christians (8%). Hindu law is very flexible and accepts anything which is good for mankind provided that it does not inflict any injury to the moral values and sentiments of others. Muslims accept ART but with reservations against sperm, oocyte, and embryo donation. Catholics morally do not accept ART. Based on these diverse religious instincts and upholding the medical decorum and human rights in a democratic manner, the current ethical and legal issues related to the practice of assisted reproduction in India are discussed in the present communication.

ART IN UNMARRIED COUPLES

By customary social practices, ART is permissible only in married couples. In some countries, such as France, Austria, and Germany (1,2), medical assistance to procreation (MAP) is also permissible for unmarried couples who have lived together for at least 2 years, though some departments ask for a certificate for "concubinage." In India, this is not permissible by law and ethics. Even if a child is born by in vivo pregnancy, in unmarried couples, by law, the child is denied inheritance of paternal or maternal property. But the welfare of the child has to be accepted by the couple by law until the child reaches the age of 18.

USE OF DONOR SPERM FOR ARTIFICIAL INSEMINATION

"Donor" implies a gift with no payment. Advertisement and payments are considered unethical.

In India, the situation is equivocal. Law does not restrict the use of AID so long as the procedure is performed with the informed consent of both partners. The donor remains anonymous, as does the recipient. An informed consent has to be signed by the donor confirming that he will have no legal right to a child born by insemination of his semen sample. Social custom demands voluntary donation without financial involvement. The donor is screened for HIV, HBSAg, and genetic diseases. Donors are usually college students and therefore come from the upper middle class, with respectable family backgrounds. The semen samples are frozen and are used after 6

months provided that the second HIV test is negative. The same donor's semen sample is not used to produce more than 10 children; otherwise there could be a probability of consanguineous marriage among the children born by such a procedure. In India, Muslims do not accept AID by religious decree, whereas there is no such restrictions among Hindus.

EGG DONATION

Donor oocytes are used in premature ovarian failure, women with natural menopause who have lost their only child, repeated pregnancy wastage with chromosomal structural abnormality, repeated fertilization failure, and poor responders in an IVF stimulation protocol.

"Birth mother" is the legal mother in English law (3). Though there is no specific law, the same applies to egg donation programs at Indian ART centers. Donors should be married women less than 35 years old and must have at least one child. Various types of donors exist—unpaid relatives, unrelated altruistic donors, or sharing of oocytes as they undergo their own IVF treatment. Human organ donation in exchange for financial coercion is punishable by Indian legislation. Though this applies to kidney donation only, oocyte donation has not yet been included under legal purview. But with regard to oocyte donation, commercialization may have some benefit. There may be no desire to keep the child, with the donor handing the child over without hesitation and not questioning who should receive her oocytes and not having a partner who himself needs counseling. But egg donation in exchange for money is not respected in India.

Whenever a child is born following either sperm donation or egg donation, not only custom but law requires that care should be taken of the newborn until he/she attains the age of "majority," which is 18 years under the statute of India. Neglect of the offspring is not penal, but when the husband and wife have signed the form of acceptance of oocyte donation in an IVF program, the courts have the power as a matter of consideration to compel the parents to take appropriate care of the child, until the child attains the age of 18 years.

SURROGATE PARENTING

Surrogacy, a procedure in which the uterus is hired, is a totally different procedure than achieving

pregnancy by egg donation. In surrogacy, confidentiality cannot be maintained in the family or in the society, though genetic parentage is assured. After the child is born, a surrogate mother may have more interest in the baby than a woman who has donated her eggs. This applies more to surrogacy, which supplies the genetic component as well as the uterus. Prevailing social custom and religious bodies (particularly the Muslims) do not accept surrogacy liberally and the law is not very clear. Commercial surrogacy is totally disrespected. Young married women with an absent uterus (either congenital or after accidental removal) may benefit from surrogacy. Sisters or volunteer surrogates are ideally accepted, with informed consent of partners on both sides.

EMBRYO REDUCTION AND SEX SELECTION

The incidence of multiple gestation in ART pregnancies is bound to increase. The obstetrical advantages of embryo reduction are many, but medical risks and ethical difficulties are numerous. The severity of medical risks seem to decrease with experience. Long-term follow-up of children from continuing sacs remains to be done.

The moral status of the conceptus after fertilization remains a major ethical argument against embryo reduction and sex selection.

In India, a human is considered to exist as recognized by prevailing religious decree, when the fetal heart starts beating i.e., approximately 45 days after the last menstrual period or 30 days after fertilization. Hence fetal reduction by existing social customs is not acceptable. But in principle and law this is allowed because it is performed for the benefit of the continuing embryos and for the welfare of the mother. In India "female feticide" was being performed for gender selection (4, 5). This practice has been legally prohibited except on medical indication (sex-linked medical disorders).

Though by religious decree, this short period of human development is generally accepted, before which a human is considered not to exist, but Indian law introduced the medical termination of pregnancy act in 1971 (6), liberalizing termination of pregnancy on either medical, social, or voluntary grounds (but not on sex-selection grounds) up to 20 weeks of gestation. Of course, this act was introduced with the objective of population control.

EMBRYO RESEARCH OR DONATION

For embryo research, approval is required by an ethical committee approved by either the Indian Council of Medical Research, the Indian Society of Assisted Reproduction, the Dean, Faculty of Medicine/Science, of a local University, or the Department of Health, state government.

The Indian Council of Medical Research is considering the following statutory guidelines relating to embryo research and embryo donation.

(1) There should be a statutory regulation whereby embryology laboratories shall have complete freedom to treat surplus embryos with the consent of donors either for research purposes or for donation to a suitable recipient without any commercial involvement in these procedures.

(2) The regulatory climate will improve if a code of secrecy and freedom of use of embryo and prohibition of commercial use is introduced.

CRYOPRESERVATION

Surplus embryos and donor sperm are cryopreserved. Oocytes are not cryopreserved. If the woman has become pregnant with fresh embryo replacement, then the surplus frozen embryos are preserved for a maximum period of 5 years, in case the woman wishes to have a second replacement. Of course the age of the woman is taken into consideration, while considering the duration for which the embryos are to be cryopreserved. For example, if the age of the woman is more than 35 years, the duration of embryo cryopreservation is reduced to 2 years. But they are never destroyed, even if the couple does not desire a second replacement. These embryos are then used for donation to infertile couples who need them (premature ovarian failure with an azoospermic husband). Alternatively these embryos may be used for research (with the approval of the local ethical committee). An informed written consent from the donor partners is mandatory. In exceptional circumstances, ownership of the frozen embryo in the event of death of one or both partners may become a controversial legal issue. In Austria, law indicates that the cryopreserved embryos are to be destroyed after the lapse of the stipulated duration (1 year), but in the same country embryo research is prohibited by law. This appears to be contradictory.

The concept of sperm cryopreservation for AID became popular in India after the introduction of embryo cryopreservation in IVF programs. Prior to this, AID was performed with freshly donated semen. There is no legal objection, but on religious grounds Muslims and Catholics, in general, do not accept the AID procedure for reproduction.

NUMBER OF EMBRYOS TO BE TRANSFERRED

By prevailing customs, the number of embryos transferred has been limited to three or four, though there is no specific law. This is only to reduce the incidence of multiple pregnancy and avoid the risk associated with the procedure of fetal reduction. Legislation limiting the number of embryos to be transferred aims at reducing the incidence of triplets to less than 2%. But there are various factors bearing an impact on the implantation rate: the age of the female partner, the ovarian reserve as expressed by day 2 FSH, the development of a new culture medium which will improve the embryo quality, the possibility of transfer at the blastocyst stage, the development of knowledge of the implantation window, and, finally, the difference in the implantation rate for fresh versus cryopreserved material. Unless these parameters are assured, the number of embryos to be transferred will remain between three and four.

INTRACYTOPLASMIC SPERM INJECTION (ICSI)

ICSI is practiced in India by at least 10 of 50 ART centers in the country. But infertile males with gross degrees of oligozoospermia or azoospermia may have a genetic trait causing concern about inheritance in the offspring. A major concern is related to the presence of microdeletions on the long arm of Y chromosomes (7,8). Azoospermic patients with congenital absence of the vas deferens (CAVD) may have deletion or mutations of the cystic fibrous gene.

Genetic screening has become a routine practice in India, especially when ICSI is performed with sperm obtained at various stages of differentiation from sources other than the ejaculate. These procedures seem to work but the patients are informed about the transmittable risk of other, yet unidentified

factors and the procedure itself is still in the experimental stage. These factors are explained to the couples before they are accepted for ICSI with MESA and TESE.

PREIMPLANTATION GENETIC DIAGNOSIS

Embryo biopsy does not grossly alter the integrity of the individuals born following this procedure (9). Preimplantation genetic diagnosis allows selection of suitable and unaffected embryos for replacement. PGD therefore avoids the risk of interventional procedures such as CVS and amniocentesis.

The procedure is being performed at more than 20 centers around the world and is currently being performed to identify single-gene and chromosome disorders. In India, except for sex selection, preimplantation genetic diagnosis is morally acceptable under existing social customs. Though about to start, the recommendation has already been forwarded to the Indian Council of Medical Research (ICMR) and has already been accepted on principle.

CLONING

The popular reaction to human reproductive cloning has been on the negative side. Yet there has been a suggestion from experts participating in the public debate on Ethical Guidelines on Biomedical Research held in Calcutta on 16 August 1998 that there is no need to impose a blanket ban on all aspects of human cloning at this point in time. Favorable developments are occurring in animal experiments and in the field of animal husbandry. Some of them might be beneficial for human health also.

PROPOSED ETHICAL GUIDELINES ON BIOMEDICAL TECHNOLOGY AND RESEARCH IN INDIA

A public debate (10) on Ethical Guidelines on biomedical Technology and research was held in Calcutta on 16 August 1998. The following recommendations were submitted to the ICMR and Indian Society of Assisted Reproduction (ISAR).

(1) Biomedical research in India should be priori-

tized in such a way that maximum benefit accrues to large numbers of people at minimum cost.

(2) The current commercialization of some organ donation in India is a matter of grave concern. Efforts should be made immediately to reduce the nature and extent of commercialization.

(3) Cultural norms, values, and traditions must be respected.

(4) Informed consent of the individual participant must be obtained.

(5) No individual should be coerced, directly or indirectly, to provide a biological sample.

(6) Safety and confidentiality of individuals must be ensured.

(7) The right to withdrawal from participation must be honored.

(8) Benefits from the research should be shared with the individual participant.

(9) Misuse of data or results of the therapy and research should be avoided and prevented.

(10) Professional competence must be ascertained.

(11) Accountability and transparency are to be audited.

In drawing up the national ethical principles, the proposal has taken into account the following existing codes of ethics: (i) the code of ethics of the Medical Council of India, (ii) the Nuremberg Code, and (iii) the Helsinki Declaration.

The ICMR or a similar body should set up a vigilance cell or a monitoring body to ensure independently or impartially that the documented ethical guidelines are adhered to in biomedical research involving human subjects.

CONCLUSION

In India, gamete and embryo manipulations have not yet entered the area of commercial or scientific exploitation. Religious and social customs are such that unmarried mothers will never come for ART, divorce is infrequent, and hence, the claim of frozen embryos by either partner after divorce has not yet embarrassed an ART center. But there should be a guideline, and the Indian Society of Assisted Reproduction in collaboration with the ICMR, and the Ministry of Health, Government of India, is trying to establish a Central Registry and an accreditation

committee, for overall supervision and accreditation of the different centers in the country.

In India, the prevailing social customs and religious practices are liberal about anything which is done in good faith for the welfare of mankind in general without inflicting any injury to the sentiment of others. Therefore, whether it is oocyte or embryo donation, surrogacy, embryo freezing, research, or even cloning, unless it is used for commercial purposes, the statutes and guidelines as existing today in India should allow facilities to expand the technological expertise in the field of human reproduction in general and ART in particular. A uniform code of conduct for ethical guidelines on biomedical technology and research is being formulated through public debates in different parts of the country.

REFERENCES

1. Cohen J: J Assist Reprod Genet 1995;12(10):663–664
2. Bernat E, Vrant E: The Austrian Act on Procreative Medicine: Scope, Impact and Inconsistencies. J Assist Reprod Genet 1993;10(7):449–452
3. Lockwood GM: Donating life: Practical and ethical issues in gamete donation. In Ethical Dilemmas in Assisted Reproduction, 1997, Vol 7, 23
4. Booth B, Verma M, Sivert Beri R: Foetal sex determination in Punjab, India: Correlations and implications. Br Med J 1994;309:1219–1261
5. Rajan VGJ: Will India's ban on prenatal sex determination slow abortion of girls? Hinduism Today 18 (http://www.HinduismToday.com/Kauai.hi.us/ashram/Apri_96.htm#gen241), Feb 1, 1997
6. Medical Termination of Pregnancy Act, 1971, Central Act/Federal Law (Act 34 of 1971). AIR Manual, 5th ed., 1989, Vol 33, p 943, published by All India Reporters Pvt. Ltd., Congressnagar, Nagpur
7. Commins J: Controversies in science: Intracytoplasmic sperm injection, ICSI, may foster birth defects. J NIH Res 1997;9:34–38
8. Tournaye H, Van Steirteghem AC: Intracytoplasmic sperm injection: ICSI concerns do not outweigh its benefits. J NIH Res 1997;9:35–40
9. Handyside AH, Kontogiania EH, Hardy K, Winston RML: Pregnancies from biopsied human pre-implantation embryos sexed by Y-specific DNA amplification. Nature (London), 1990;244:768–770
10. Extract of public debate on Ethical Guidelines on Biomedical Research, Calcutta, Aug 16, 1998

B. N. Chakravarty

Institute of Reproductive Medicine
Salt Lake
Calcutta, India