The health of children conceived by assisted reproduction technologies

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The provision of assisted reproduction technologies needs to operate within a defined ethical framework that safeguards the welfare of all concerned

Assisted reproduction technologies (ART) account for the conception of around 1% of children born in the UK each year (over 10 000 children).^{1,2} The primary purpose of ART is the treatment of infertility and the conception and safe delivery of healthy children with the potential to become healthy adults, but some techniques permit embryo selection and testing.^{3,4} As the range, application and success rates (live births per treatment cycle) of ART have increased, so their consequences for the children produced have become more apparent. Since paediatricians have moral obligations to maximise children's welfare and to act as their advocates,⁵ they may have reasonable concerns about the health and welfare of the increasing number of children conceived by ART.

THE OBLIGATION TO CONSIDER THE HEALTH OF CHILDREN CONCEIVED BY ART

Children born alive have full protection in law that imposes enforceable duties, including that of meeting children's health needs, on those with parental responsibility.⁶ Although this legal protection does not generally extend to embryos and fetuses, those who provide ART have ethical and legal duties to consider the welfare of children born as a result (the welfare principle).⁷ This duty can be interpreted as being limited to considering whether there are any adverse factors which might preclude a particular couple from becoming parents. However, the welfare principle also entails consideration of what adverse health outcomes for children may be associated with use of ART and how they should be ameliorated.

HEALTH OF FUTURE CHILDREN AND PARENTAL FACTORS

Desperation associated with infertility may lead would-be parents to take risks with both their own and their future child's health,⁸ but these – and professional

discomforts about their motivation to become parents – may be insufficient reasons to deny them ART. However, because of their proven risks to children some medical conditions (genetic or infectious diseases) and social factors (ongoing substance abuse, domestic violence, severe mental impairment and history of preceding child abuse) are generally regarded by our society as acceptable reasons for denying couples access to ART. Other issues, for example marital status or sexual orientation, reflect society's perceived family ideals rather than proven risks or morally relevant principles,^{9,10} although further case-controlled studies on psychosocial outcomes may be required to confirm this view. Any reasons for denying couples access to ART must be transparent, based on appropriate moral principles and reliable scientific data, and applied equally and fairly to all.

ADVERSE HEALTH OUTCOMES ASSOCIATED WITH ART

The greatest risks to children conceived by ART arise from the increased incidence of multiple pregnancies^{11,12} caused by the implantation of several embryos to achieve better chances of conception.^{1,2,13} Multiple births are associated with prematurity and low birth weight and their concomitant social and economic costs related to long-term health and neurodevelopmental sequelae,¹⁴ and with increased mortality and morbidity for mothers and babies. Parenting high order multiples also carries risks of stress and relationship dysfunction.

Such births also increase competition for scarce neonatal intensive care (NIC) resources. Those conceiving naturally will be unlikely to have had the option to limit their risks of multiple births or prematurity, whereas these may be foreseeable and potentially preventable risks of ART. Moreover, total direct NIC costs for ART twins and triplets are substantially greater than for singletons, even if long-term additional costs, for example those

pertaining to health or education, are ignored.¹⁵

Reducing the risks of multiple birth and prematurity by limiting the number of embryos implanted is therefore ethically justified because it reduces mortality and morbidity and potentially enables greater access to scarce resources for those who need it. There is increasing evidence that elective Single Embryo Transfer (eSET) can achieve benefits in terms of reduction of multiple deliveries, without significant compromise to implantation success rates.¹⁶ Accordingly there has been a recommendation to the UK's regulatory body, the Human Embryology and Fertilisation Authority (HFEA), that ART clinics should reduce their twin pregnancy rates and that eSET should be offered in the first instance to those with the best prognosis of conceiving, but this is not yet standard practice.¹⁶ Even if this recommendation is accepted, individual providers may still implant more than one embryo if they deem it in the woman's best interests to do so. Moreover, any HFEA guidance does not apply to unlicensed clinics or those in countries where implantation of several embryos is still common practice.

Avoiding multiple births will not avert all harms since ART singletons also have increased risk of low birth weight¹² and may have a higher incidence of cerebral palsy.¹⁷ Other harms may be less easy to predict or prevent, including an increased incidence of major (sometimes multiple) birth defects and of early hospitalisation.¹⁸ However, it is difficult to disentangle the effects of ART per se from those of infertility, since children conceived by ART do not seem to have a greater prevalence of congenital anomalies than those of infertile couples who eventually conceive naturally.¹⁹ The long-term effects of such embryo-invasive techniques as intra-cytoplasmic sperm injection (ICSI) and preimplantation genetic diagnosis (PGD), the latter involving the testing of single cells removed from embryos, are not yet defined. Other physical harms, for example growth problems, may be related to embryonic environment and manipulation, or inherited from parents, for example adult infertility.

Most studies have shown that children conceived by ART are not at greater risk of problem behaviours, nor do families show signs of parenting stress, at least in the short term.²⁰ Identified psychological harms mainly relate to conflict over the rights of donor-conceived children to know their own identity.²¹ Despite a greater culture of openness (marked in the UK by the provision that as of April 2005 gamete donation can no longer be

anonymous), the majority of heterosexual parents do not tell donor-conceived children the circumstances of their conception, whilst many donors wish to remain anonymous. It is equally unlikely that heterosexual couples, conceiving by in vitro fertilisation or other forms of ART, will inform their children of their mode of conception. The long-term effects of being a saviour sibling are also unknown. However, unplanned revelation of family secrets can produce unhappiness, anger and confusion for all concerned.²¹ These issues are of ever greater importance as the number of children conceived by ART grows.

Choices involved in the use of ART are increasingly complex and entail sensitive value judgements. Decision-making may best be facilitated by providing prospective parents with sufficient high quality information about the likely outcomes of ART so that they can make appropriately informed choices. However, the fact that the parents' decisions are informed may not be sufficient to protect the welfare of the resulting child. Therefore, an objective professional standard may still be necessary and some robust process of data collection would inform this.

DEFINING OUTCOMES FOR ART BABIES

Obtaining information about outcomes for ART-conceived children can only be achieved by appropriate case-controlled studies of physical health, developmental progress and emotional well-being that extend into adult life.²²⁻²³ Such studies need sufficient power to enable outcomes of specific treatments, for example PGD, to be defined and need to include children of infertile couples who conceive naturally. Their ethical justification lies in their benefits to individual children and the provision of information to inform choice in those contemplating ART. It is also important to counsel infertile couples sensitively about the effects of infertility per se on their possible children.

Obtaining details of pregnancy outcomes and the presence of birth defects is unlikely to yield sufficient information for this purpose. Intermediate follow-up requires linkage from existing databases to those providing routine health data and would require research ethics approval and would be addressed by UK Government proposals to reform the Human Fertilisation and Embryology Act.²³⁻²⁴ The importance of collecting personal information for public good is emphasised and justified in a report from

the UK Academy of Medical Sciences.²⁵ The report makes recommendations for improving regulatory processes governing such research, the development of good practice guidelines, harnessing NHS national IT programmes and greater public involvement. Such an initiative, with appropriate safeguards, may be important in obtaining outcome data for ART children that are currently lacking.

Studies to obtain information on the long-term outcome of children involving direct contact with families would still require scientific peer review and ethical consideration. Difficulties in obtaining parental consent for such studies might be anticipated because of the implicit need to make older children aware of how they were conceived. Such difficulties may be minimised by designing patient-based studies within a framework that recognises the views, priorities and rights of all concerned. If this were done, it is likely that many people seeking ART would participate.²³ Paediatric expertise in the design of such studies would be important. In the meantime, it seems reasonable for paediatricians to make sensitive enquiries about a child's mode of conception in clinical circumstances where this seems appropriate.

CONCLUSIONS

The provision of ART needs to operate within a defined ethical framework that safeguards the welfare of all concerned. Those contemplating ART must be sufficiently informed of both the risks and the benefits to themselves and future children so that they may exercise autonomous choices. Children born by ART have the right to expect that their parents received appropriate information about risks and the actions that might be taken to prevent or reduce them, and that a fair balance was struck between their parents' liberty rights and their rights to protection.

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