ETHICAL DILEMMAS IN ART: CURRENT ISSUES

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Most treatments in assisted reproduction raise ethical issues, and it is difficult to be exhaustive and detailed. Nevertheless, the aim of this chapter was to highlight the main ethical concerns that have been discussed since the inception of the complex, although now routine, technique of IVF. That the human embryo could be observed outside the body captured the world's imagination, in a different way than, for instance, the less technically taxing but older techniques of sperm donation. This had also led to many debates, and so do eternal themes, which return only because of the use of more modern technology like social sex selection. This chapter will cover gametes donation for reproduction and research, including embryo research and the newer issues around stem cell research, a subject of major current interest, rekindled by the therapeutic hopes from the possible use of embryonic stem cells, with or without somatic cell nuclear transfer technology (SCNT). Furthermore, the complex choices to be made in the use of preimplantation genetic diagnosis (1) are also the matter for ethical debate, and finally, one should not avoid the international concerns about sex selection for social reasons, an issue that has implications far outside the specialist field of ART. Other more specialized issues, from the cryopreservation of reproductive tissues (2) to the use of posthumous gametes (3), have been included in previous publications.

Thus, the choice of emphasis in this chapter is necessarily eclectic, but one should start with an issue relevant to care in general, in particular, access to treatments and justice. Access to fertility treatments is far from equitable worldwide as some countries will only provide private or restricted treatments. Restricted access to IVF, however, occurs not only in resource-poor countries but also in some wealthy countries. One may thus contrast France and the UK, with their number of IVF cycles and funding policies vastly differing (4), and certainly, the UK postcode access to IVF treatment, with its double pronged iniquity (5), is an example that is still now relevant to daily practice.

GAMETE DONATION

Two main issues surround gamete donation: the traditional and more recently questioned anonymity of the gamete donor, which must be put in the context of the sense of identity of the offspring in relation to that of his/her intended (or psychosocial) parents and to his/her origins and; the other issue, older still, but often rekindled especially when donation becomes scarcer – should donors be paid, an oxymoron (6), or compensated for their donation and what is fair compensation?

Furthermore, the fact that sperm donation has been used for many years means that we have more evidence about the follow-up of children born from this method than for the offspring of oocyte (or embryo) donation, two techniques requiring the use of IVF. But before analyzing what is relevant to knowing one's origins, mention must be made of the issue of payment or compensation of the donors.

It seems obvious, at least from a semantic point of view (7), that a gift should be free. Indeed, the fact is that if society intends to pay gametes donors, the term "donation" itself should be changed to "sale" of gametes and embryos.

However, in most countries where gamete donation is used as a means of solving infertility problems, those who recruit the donors have difficulties matching the supply to the demand, especially in the case of oocytes. Thus, it has been argued that pragmatism should prevail in a scarce supply environment and that some type of financial inducement should certainly not be forbidden. In the UK, this, of course, must be within the frame of English law, which states that "no money or other kind of benefit shall be given or received in respect of any supply of gametes or embryos unless authorised by directions" (8). The notion of gifting is also enshrined, among others, in the law in France and Spain, although there compensation is given as a lump sum to egg donors.

With the conviction that the human body and its parts and products should remain outside commerce, one can attempt a rational argument in the realm of ethics, in order to outline the theoretical basis to altruistic donation. The special respect due to the person was most cogently articulated more than 200 years ago by Immanuel Kant. It stems from the observance of the second formulation of the categorical imperative, "to treat all humanity always at the same time as an end and never merely as a means," and is understood in modern terms as a prohibition of commercialization of the human body and its products.

The opposite utilitarian attitude has proposed that in a scarce-supply environment, one might choose to pay donors. But negative consequences identified by Titmuss about the payment for blood donation can be applied to gametes donation: this may deter genuine altruistic donors (9) and there may be an increased risk of transmitting disease by donors motivated by gain only and willing to falsify information and, especially, the risk of potential exploitation of the weakest socioeconomic groups of society (10). This very argument of potential coercion is that used by opponents to egg sharing, a pragmatic approach used in the UK to increase oocyte donation, and

indeed the only possible way to donate oocyte in Denmark, in order to protect women from taking the risks of stimulation and egg retrieval they would not otherwise ensue. The HFE Act 1990 allowed benefits for female donors (those allowed being treatment services and sterilization), and the debate can be thus summed up: is this a form of coercion to donate or a form of payment or is it an acceptable "exchange"? An objection to the practice has been that it may compromise the chance of success of the donor, but her selection (young, with polycystic ovaries, and a male problem, for instance) may obviate this. Therefore, a perhaps even harsher dilemma involves the potential egg sharer who is refused because she is too old or has a prejudiced ovarian reserve, especially if she finds the cost of the procedure difficult to bear. It goes without saying that the counseling in such cases is even more complex, time consuming, and essential, as recommended in the UK by the HFEA code of Practice (11). But the main objection remains this intrinsic to the fact that the practice may be regarded as payment (12): indeed, there is now some evidence from Belgium about the degree of financial necessity, if not coercion, that may apply (13) as the number of women volunteering to share declined sharply after Belgium insurance became more generous of reimbursment of cycles.

Concerning the theme of anonymity, a recent change in UK law highlights the complexities involved: since 2005, similarly to Sweden from 1985, all new gamete donors must undertake to give their name at the offspring majority (14). Whether this will deter new donors, especially egg sharers who would find out eighteen years later that their recipient was successful, and if they were not, time only will tell, although national figures collated by the HFEA already show a decrease in number of donors in 2005.

New studies concerning children who have been told of their origins will offer evidence on the lack of secrecy of the procedure of gamete donation, but we may have to wait a long time before being able to observe the effects of known donation on children. The question is the meaning of knowing one's origins, a matter of importance to each and everyone of us, but one that has many different meanings, historical, psychological, and anthropological, while arguably the meaning of genetic origins is newer to humans than that of kinship in general.

Powerful voices of anger and distress of some children of sperm donation have been heard (15), arguing that they have been deprived of specific knowledge, the identity of the genetic sperm provider (avoiding the legal and emotional term father), information without which they do not find their sense of identity complete. We know, however, that in most cases, the interests of children and parents seem to coincide as several studies have already shown that children conceived by "assisted reproduction" fare very well in several measured personal and social criteria, when compared to children conceived "naturally" or adopted (16). Another argument used is that of "the right of the child" to know his/her "origins" and the potentially divisive role of secrets in families. When one enters the area of rights and finds a conflict of interests between those claiming rights, it is difficult to ascertain which one of them might take precedence. In this particular case, do we, for instance, prioritize the "right to privacy" of the parents and donors or the "right to know" of the prospective child. Thus, balancing parental choice, which is generally assumed to be benevolent to the offspring until proved otherwise, and children's interests, the European Society of Human Reproduction and Embryology (ESHRE) taskforce

recommendations (17) upheld the double-gate system, recently rescinded in the Netherlands. This system enabled parents and donors to choose or not choose the disclosure of identity later and to match thus prospective parents and donors. The fact that we have no evidence that the outcome is not generally at least as good as that of naturally conceived offspring is reassuring, but we must not forget our (ethical) responsibility to these children as a profession and indeed our (legal) duty of care, whether general or specific, as it is in UK law. It is indeed our duty to look prospectively and reflect on different approaches. For the time being, it seems that democratic openness to different approaches in families and the respect of their privacy favors a double-strand approach (18), with all the consequences for the children for whom we are jointly responsible.

PGD, WITH OR WITHOUT HLA MATCHING TO CHOOSE A SAVIOR SIBLING

Ever since it was first practiced, preimplantation genetic diagnosis (PGD) has evoked the fear of potential genetic manipulation and been criticized as a step on the slippery slope to criminal eugenics (19). If eugenics is defined as a practice imposed on a population and not in terms of individual couples' choice to avert possible serious disease (cystic fibrosis, for instance), this accusation can be refuted (20). Other fears voiced were whether it would lead couples to expect the assurance of a "perfect" baby, while all they wish for is a normal child, not affected by grave familial disease. But most questions are similar to those encountered in antenatal practice, when screening, and it may be argued that PGD could be called "pregravid diagnosis," enabling couples with serious genetic disease to avoid the suffering of deciding to terminate an affected pregnancy, while also taking on the burden of going through IVF when they are most often fertile. Their decision is enabled through information, including genetic counseling, a key to their autonomy. The aim of an unaffected pregnancy takes into account the welfare of the future child, an essential criterion in our specialty (21).

A newer dilemma is that of choosing by PGD an embryo free of a disease to facilitate the birth of a savior sibling, a child who would be an HLA match for a very sick older sibling (22).

The main argument against this kind of request by the parents is the instrumentalization of the future child. This dilemma is illustrated by two different cases that originated in the UK: either the child conceived by PGD and embryo transfer (ET) is also at risk of the genetic disease affecting the older sibling, as for the Hashmi family, or this future child has no such risk and PGD is solely performed for HLA typing, as for the Whittaker family.

In the UK, each PGD case must be licensed by the HFEA, and the Hashmis' request was accepted as they wished for an embryo to be matched to their seriously ill son with thalassemia, for whom all other treatment had become ineffective. However, the Whitakers' was refused because their sick child suffered from Diamond-Blackfan anemia, a disease that is mostly nongenetic, and thus the future planned child was not at risk of this condition and would be planned perhaps "merely" to save the older sibling. After much public debate, and a successful PGD in Chicago resulting in the birth of a savior sibling, the HFEA stated the following year that further similar cases would be licensed in the UK. Thus, the danger to the life of the existing sibling serves as the compelling reason to accept the technique. Even from the point of view of the

future child, it may be seen as beneficial to be able to save its sibling as a matter of solidarity and seems acceptable if the future child's operation involves minimal risk (e.g., cord blood or bone marrow donation). Practical issues inform the consent obtained from the parents, like the fact that cord blood donation is only possible if the affected child weighs less than 25 kg and the fact that the technique is less likely to give results if the woman's age is thirty-eight years or more (23). In all cases, counseling may help the parents to foresee difficult events, as the failure of the initial aim, for instance: what if there is no embryo to match the sick child and what if the planned child does not save the life of the elder sibling?

Another problem concerns the acceptability of the motive for the selection of embryos: there the "postnatal" test is useful as it states (22) that it is ethically acceptable to enable the birth of a child by PGD/HLA who can be used for a certain goal if it is acceptable to use an existing child for the same goal (i.e., if it is acceptable to volunteer an existing child for stem cell donation to a sibling and if it is acceptable to enable this birth by PGD/HLA). But the creation of a child for the purpose of harvesting non regenerating organs seems extremely difficult to justify in view of the risks involved for the donor child, and adults' self-interest is unacceptable (i.e., not for parents themselves).

Finally, some have specified that this solution is morally acceptable if the use as a donor is not the only motive for the parents to have the child; but parental motivation is particularly difficult to assess (23), and thus, the postnatal test is preferred, as long as the parents "intend to love and care for this child to the same extent as they love and care for the affected child."

CLONING AND THE USE OF EMBRYO'S STEM CELLS

Let us first dispose of the issue of human reproductive cloning: in articles and comments (mostly) condemning reproductive cloning, words like dignity, identity, sameness, and the moral sense of "self" have been analyzed at length (24), not withstanding the fact that the technique is far from safe, which provides the main and overwhelming objection. One may also object on the grounds that reproductive cloning would threaten the autonomy of the future cloned person who may be treated by society as somewhat predetermined, entailing as it does an increase in (genetic) determinism even if relative as the clone is born into another environment than the person replicated. Safety and the psychological arguments seem to be the only arguments worth opposing the proponents of reproductive cloning: the narcissistic venture of the parent(s) may well threaten the building of the identity of the child, mostly by decreasing the possibility of separation from the initial model and thus his/her autonomy.

It is with this in mind that the ESHRE issued a statement "to continue the ban on reproductive cloning," after a five-year voluntary moratorium on reproductive cloning in 1999, when it became clear that technical advances arising from cloning animals could theoretically result in an attempt to clone a human.

Fortunately, the repulsion caused almost universally by reproductive cloning has not been universally matched by the same feelings or arguments concerning the use of stem cells from human embryos. Indeed, UK was the first state to allow therapeutic cloning (25): embryo research has been licensed

under strict conditions since the HFE Act 1990, permitting only research linked to reproduction. After a democratic process involving a report by the chief medical officer and a vote in both chambers, new categories were added to statute January 31, 2001, allowing this time "research for serious disease." In all cases, though, the vexed question of the status of the human embryo has been rekindled.

Thus, aware of the potential exploitation of semantic games when discussing embryo research in general, the ESHRE task-force defined the preimplantation embryo in its first ethics consideration on behalf of the society (26). The taskforce stressed that this term was descriptive, meaning the embryo out of the body before it is given a chance of becoming a fetus and then a legal person by ET. But such a descriptive term does not imply a lesser quality.

Meanwhile, specific issues arise from the possible application of stem cells animal research to the human embryo.

Many fundamental ethical questions in this field are far from new. Indeed, consent must be obtained for research, reflecting the principle of autonomy. But the taskforce stresses "in view of the special nature of stem cells and their longevity, it should be specifically mentioned that the embryos will be used for research into the establishment of cell lines which can be kept indefinitely, may eventually be used for therapeutic purposes, and will never be replaced into a uterus. It should also be made clear whether the cells may be used for commercial and/or clinical purposes," making consent more specific than general.

There are also specific ethical considerations according to source of cells and especially regarding the creation of embryos specifically for research. Indeed, this question of the creation of embryos for research is especially vexed. While article 18 of the European Convention on Human Rights and Biomedicine (27) specifically forbids this, in the UK, the HFEA is charged with overseeing embryo research within the legal limits, by a licensing system: the creation of embryos de novo for research is not unlawful, but its "necessity" must be demonstrated, ensuring that embryos are not created for futile reasons, that indeed this creation de novo is licensed only if the information cannot be obtained by research on supernumerary zygotes.

Furthermore, in practice, the source of oocytes used for any embryos created (especially by SCNT) is a major problem, for two reasons. First, the already well-documented imbalance between needs and supply in the case of egg donation for reproductive purpose. But of special concern is the potential abuse of vulnerable women who might be enticed to sell their oocytes. Indeed, recent publications (28) have questioned the conditions of oocyte donation for research and the pressure put on women to take risks when "compensated" for their "gift". Interestingly, however, there was little mention of the compensation to women giving oocytes for reproduction, when this is sometimes far beyond this recommended by the ASRM ethics committee (29). This could be called the oocyte paradox, where value seems to vary according to the use to which oocytes will be put. It is possible that the concern of payment in this case reflects the fundamentalist stance on the status of the embryo, expressed by those opposed to the creation of embryos for research in general, rather than a concern for the women

Several statements (30, 31) already highlight the issues that came to public notice with a vengeance when it was realized that the Korean experiments were not only faked but also breached the autonomy of women who had been coerced into giving their oocytes in the project, cumulating most possible sins to be performed in research (32).

Furthermore, as transborder iniquities may be worse than national ones (mostly for reason of sometimes great economic disparity), avoiding recruiting women abroad for egg donation might be a solution, even partial, to this problem (31).

SEX SELECTION FOR SOCIAL REASONS

The matter of gender social selection, which we discuss here within the frame of ART, is not novel in historical terms: baby girls have been exposed on the hill side to die from time immemorial and female and adolescent children submitted to negative discrimination in health and education of old in many societies. But the availability of technology, whether low key (sperm selection) or complex and intensive (PGD), has rendered the efficacy of sex selection more accurate and therefore less innocuous than the old mythology of having sex at a certain time or ingesting a special regime at conception in order to achieve the desired effect.

The facts are still that at the worldwide level, the practice of gender selection is more often to favor the birth of a son rather than a daughter (33, 34) and is, therefore, a women's rights issue. But in order to be nondiscriminatory against either sex, this debate is placed within the Human Rights context. This framework stresses its political connotation, as well as the ethical aspects, within the context of a universal rule and against cultural relativism.

The background is that of gender inequality worldwide, and as the social anthropologist M. Strathern said in 1993 "it is worth asking whether making (sex selection) acceptable to select one sex in preference to another at the moment of conception will make it easier or harder to promote anti-discriminatory measures in other areas of life" (35).

Indeed, gender discrimination is common worldwide and can have many guises. The obvious imbalance of sex ratio observed in areas of India (34) and China (36) is one extreme piece of evidence of its occurrence. In India, where A. Sen recently concludes that "reduction in female mortality has been counterbalanced by sex selective abortions," evidence has been surmised from a survey of births in 1.1 million households (37), concluding that the imbalanced ratio stems from the use of prenatal ultrasound gender diagnosis followed by TOP [Sheth (38)], although India passed in January 1996 the Pre-Natal Diagnostic Techniques (Regulation and Prevention of Misuse) Act. This had little effect, till recent years, as only 300 practitioners have been sued in India, with the medical profession accused of "arrogance." However, the jailing of Anil Sabhani in the state of Haryana may, represent a turning point (39). We know that worldwide, prenatal sex determination is performed with a view to terminate a pregnancy of the "wrong" sex merely for social reasons; this is actually in most legislations an illegal abortion. For instance, the Canadian example shows, however, how some women (mostly of Indian origin) cross the border to the United States to have fetal sex determination and return for a TOP in Canada, if the child is of the unwanted sex, when this is still acceptable within legal limits for "distress" (40).

China faces similar bias in some regions (36), but dissenting voices are coming from the National Institute of Philosophy, which declared in June 2004 that it was time to act and

recommended, in particular, the licensing and monitoring of the use of ultrasound machines and especially the application of existing laws against gender discrimination.

Till recently, some European countries were allowing by defect the seemingly innocuous methods of sperm sorting for couples to choose the sex of their offspring because only ART methods were covered by legislation. In such countries, discrimination is measured in general by educational and economic analysis rather than by sheer number of men and women but is nevertheless still a sizeable problem. However, recent national debates in Belgium and the UK have resulted in the banning of social sex selection, and the advice that evensperm sorting by flow cytometry should be subject to regulations (41), confirming that moral appraisal of such a grave issue does not depend on the method used. This contradicts the "gradualist" view that gender selection by PGD, or termination of pregnancy, is worse morally than if performed by a simple technique like sperm sorting. The logic there is that discarding an embryo for being of the wrong sex is a lesser evil than a TOP as the fetus is even nearer achieving its potential (at least legal) personhood and itself less serious than sperm sorting.

Over the Atlantic, although the American Society for Reproductive Medicine Ethics Committee found highly problematic the use of gender selection, it did not strictly condemn the principle.

But a comment by the advocate of reproductive rights demonstrates uneasiness: Robertson says that techniques for sex selection (42) although not to be "legally prohibited" or "morally condemned" should be "not encouraged" or even, in some cases, "actively discouraged" and concludes that only gender balancing is acceptable (43). This compromise (44) that allows choosing the sex of the second (or more) child only providing it is different to this of the first, interalia, was also presented in the ESHRE ethics taskforce on PGD (21), with the alternative of the totally disapproving and strict Human Rights view. To accept family balancing, however, implies that sex selection is not sexist per se or that the social consequences (in the sense described by M. Strathern) do not warrant such a sacrifice to procreative liberty.

Therefore, we would like here to stick to the strict view, holding that any kind of selection, whether called balancing or not, is inherently sexist; furthermore, a family of only boys or girls is not imbalanced, a negative qualification by comparison with the supposedly ideal boy and girl "balanced" family.

Indeed, some arguments trying to justify sex selection as a reproductive choice are worse than others. For instance, the known imbalance of sexes already existing in some societies has led to comments that this would lead to an increased "value" of females, a demeaning attitude for whichever gender becomes thus of "scarcity value." This terminology of the market place reduces further the status of women (in practice rather than men) to mere chattels.

Furthermore, one may argue even further that the issue is too important to reduce it to national boundaries: to the question, "does the practice of social sex selection in India justify prohibiting social sex selection in the UK?" (45), the answer is a resounding yes because the very value of Human Rights reside in their universal/international application (46).

Indeed, the whole history of human rights has been one of political reaction against injustice by discrimination on grounds of sex (as well as religion or phenotype), toward agents or groups (represented here by women as a group).

Finally, one must add that if any method, whether of low or high technology (sperm sorting versus PGD) is used to prevent disease or suffering, as in X-linked genetic disease, to be of the "wrong" gender in the eyes of one's family or of society, whether male or female, cannot be defined as a disease.

Without pointing out the obvious (a child knowing of the method used for his/her conception may have the feeling of "being conditionally wanted" and/or feel even more intense pressure than usual in her/his society to fulfill to a gender stereotype in behavior, profession, and private life) and without raising the specter of eugenics and the worn slippery slopes' warning, one may also feel that children would benefit to be born in a society where acceptance rather than rejection of any difference (of phenotype, gender, or disabilities) is the norm. It would be ideal to live in societies where the protection offered by Human Rights has become redundant, but there is no evidence as yet that this ideal is within reach.

So in practice, what can be done to slow if not stop this discrimination, which even starts before the birth of the female, as (47) "gender (is not) a serious handicap worthy of termination or selection." One may be hopeful after the case in India, and also hope that for China, the program "Action of Care for Girls," will be applied, especially in rural areas, as stated by the Institute of Philosophy.

Indeed, regardless of personal or cultural motivations, the message sex selection for nonmedical reasons ("including balancing") sends to broader society and the world at large is the suboptimal worth of women. The stakes are too high to allow any compromise till equality of opportunity (lack of discrimination) between the sexes is shown to be really implemented as demanded by Human Rights declarations. Maybe then, and only then, might one reconsider the possibility of gender balancing in families, although it is doubtful that by then many families will still be interested.

CONCLUSIONS

The discussion of these few dilemmas has implications at national and international levels, as do many others in our specialty. However, the individual dimension is often the most poignant, and this is the one practitioners certainly face in their daily practice. Nevertheless, international comparisons with the study of different sociocultural approaches help us to challenge dogma, a very sane attitude when one keeps in mind Wittgenstein's definition of philosophy, applicable to ethics ("philosophy is not a doctrine, but an activity with the aim to logically clarify one's thinking").

The interdisciplinary approach also allows us to best take into account the welfare of the future child, with the invaluable help of psychologists and counselors, especially those specialized in family dynamics.

Finally, a word about the law. According to Bernard Dickens, "Ethics frames the law within which law is voluntarily obeyed" (48). This is a final plea for debate and information before legislation is passed without bias or prejudice in all field related to ART.

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