Evolving ethics in medically assisted reproduction

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Ethical problems arising from the application of assisted reproductive technology are discussed for four specific areas, namely embryo research, multiple pregnancies, preimplantation genetic diagnosis (PGD) for social sexing, and finally PGD with HLA typing.

Key words: embryo research/ethics/HLA typing/multiple pregnancies/preimplantation genetic diagnosis/social sexing

Introduction

The application of assisted reproductive technology is replete with ethical problems. Four topics are outlined in which some morally relevant developments have occurred in recent years. Embryo research, and the perennial conflict about the moral status of the embryo, is crucial for the development of the technology in general. Although embryo research has been around for decades, it remains a contentious issue that is rekindled each time new procedures are proposed for which the use of embryos is requested. At present, embryo research is pushed to the forefront because of the development of stem cell research, including experiments with embryonic stem cells. This review firstly provides an update of the philosophical discussion on embryo research.

In the last 5 years, we have witnessed a steady increase in the interest in multiple pregnancies. More and more practitioners are aware of the serious health risks both for the children and the mother. While the reputation of assisted reproductive technology was originally threatened by its low success rate, the technology is increasingly criticized for the far too high multiple pregnancy rate. Slowly, the need for change has been recognized.

The advent of flow cytometry for preconception sex selection circumvented some arguments against sex selection and thus reopened the debate on the acceptability of applying the technique for non-medical reasons. However, the main alteration is the policy of some centres to perform preimplantation genetic diagnosis (PGD) for social sexing. The discussion and some compromise solutions are reviewed.

The last topic is linked to the previous one. A specific and relatively rare application of PGD, i.e. typing embryos on their HLA type, is analysed. However, this application, like social sexing, indirectly touches upon the original justification of performing PGD, i.e. preventing the birth of handicapped children. Increasingly, the indications are broadened to include intermediate and social reasons. It can be predicted that increasingly complicated cases will present themselves. A nuanced ethical approach is needed to do justice to such cases.

Embryo research

The introduction of new assisted reproductive technologies is closely related to preclinical research with human preimplantation embryos, aiming at investigating the safety, reliability, and effectiveness of the respective techniques. The embryos used may be either ‘spare’ embryos or embryos created expressly for research purposes. Preclinical embryo research is highly controversial, mainly because the embryos involved are used ‘instrumentally’. The fundamental controversy is whether or not preimplantation embryos have the same moral status as children or adults, who are to be protected from ‘destructive’ research.

At one end of the spectrum, it is argued that embryos, being ‘non-persons’, have no independent moral status; whether they should be treated with respect and care solely depends upon the preferences of the providers of the gametes (McCullough and Chervenak, 1994). The implication of this view is that if the embryos are not (no longer) part of a ‘parental project’, and the providers consent, the research use of embryos is considered to be morally indifferent. At the other end of the spectrum, it is argued that the embryo is a person ‘from the moment of fertilization’ or, while not yet an actual person, should be treated and respected as a person because of the inherent potential to develop into a person— the ‘strong’ version of the so-called potentiality argument (Congregation for the Doctrine of the Faith, 1987; Iglesias, 1990). As a consequence, preclinical embryo research is dismissed as criminally irresponsible. Most ethical theories, however, hold that whereas preimplantation embryos do deserve some protection, they need not be respected as persons (Hursthouse, 1987). Arguments in favour of this intermediate position vary substantially, and include moderate versions of the potentiality argument, and the view that the embryo has a symbolic value, which...
precludes its destruction for trivial reasons (Dunstan, 1984; Strong, 1997; Green, 2001).

Most ethics committees who have studied the current issue conclude that the preimplantation embryo has a relatively ‘low’ moral status and, accordingly, that research with preimplantation embryos can be morally justified, at least within some constraints (Ethics Advisory Board, 1979; Warnock report, 1984; Gemeinsame Arbeitsgruppe, 1985; Health Council of The Netherlands, 1986, 1998; Royal Commission on New Reproductive Technologies, 1993; National Institutes of Health, 1994; ESHRE Task Force on Ethics and Law, 2001). Clearly, an absolute prohibition of embryo research would be at odds with the societal acceptance of, for instance, the disposal of spare IVF embryos and the use of intrauterine devices (IUD), which seem to work, at least partly, by preventing the implantation of embryos (Stanford and Mikolajczyk, 2002).

There is a ‘strong’ consensus regarding the procedural conditions to be met: both the informed consent of the ‘parents’ (the providers of the gametes), and the approval of an (national) ethics committee are widely considered to be absolute prerequisites. There seems to be less consensus with regard to the material conditions to be imposed. While there is broad support for the principle of proportionality, which demands that the aim of embryo research should be to benefit human health, there is difference of opinion concerning the way in which this principle should be made operational. Most commentators and ethics committees insist that embryo research can only be justified if direct clinical benefits are reasonably to be expected. Others, however, argue that basic research may be acceptable too (ESHRE Task Force on Ethics and Law, 2001). Furthermore, while embryo research is (has been) restricted to research related to human reproduction in a number of countries, this limitation is increasingly—and rightly—disputed (Health Council of the Netherlands, 1997; Human Genetics Advisory Committee and Human Fertilisation and Embryology Authority, 1998). The isolation of human embryonic stem cells (hES cells) for research into cell replacement therapy in this context operates as a catalyst (De Wert et al., 2002). A second condition widely accepted is that embryos may only be used in research if there are no good alternatives—the principle of necessity or ‘subsidiarity’. But again, there is dissent regarding the interpretation of this principle, which is especially clear in the context of evaluating proposals to isolate hES cells for research into cell replacement therapy: against the restrictive viewpoint that embryos may only be used as a source of hES cells if there is proof that adult stem cells are not optimally useful, there is the more permissive viewpoint that hES cell research may, and indeed should, take place so long as it is unclear whether adult stem cells are complete or even partial alternatives (De Wert and Mummery, 2003). A third condition regards the time limit to be respected. Most committees and regulations set a time limit of 14 days after fertilization. One of the arguments in favour of this position concerns the absence of so-called developmental individuation of the embryo (Grobstein, 1988; McCormick, 1991). Some ethicists and ethics committees, however, have argued that research beyond the 14 day limit need not be categorically wrong (Council for Science and Society, 1985; Harris, 1985; Tauer, 1985; De Wert, 1987; Sass, 1989; Steinbock, 1992). They argue, for example, that research might be morally justified as long as brain activity and/or ‘sentence’ is completely absent. Clearly, this issue will remain rather academic, as long as it is technically impossible to culture embryos beyond one single week.

A major point of controversy remains the origin or source of the preimplantation embryos to be used in research. It is widely felt that creating embryos especially for research purposes is ethically (far) more problematic than using spare embryos in research (Health Council of the Netherlands, 1986; Annas et al., 1996). The ‘Convention on human rights and biomedicine’ of the Council of Europe (1996) completely prohibits the former. Others, however, doubt whether, or even deny that, there is a fundamental moral difference between the two practices (Ethics Advisory Board, 1979; Warnock report, 1984; Harris, 1989; De Wert, 1987; National Institutes of Health, 1994; Health Council of the Netherlands, 1998). Not only is the embryo used instrumentally in both cases, also the moral status of the embryos is identical. Some commentators stress that the intention at the moment of fertilization is fundamentally different (Annas et al., 1996). This difference is, however, only relative. Even in the context of regular IVF, not every embryo is created as a ‘goal in itself’. The goal of IVF is the solution of involuntary childlessness—the loss of some spare embryos is calculated beforehand (De Wert, 1987; Iglesias, 1990).

When embryonic stem cell research is proven to have therapeutic value, larger numbers of oocytes will be needed (Cohen, 2000; ESHRE Task Force on Ethics and Law, 2002). The acceptability of creating embryos for research is being questioned out of concern for the autonomy and the interests of the women donating oocytes for research (Raymond, 1987). After all, women have to undergo hormone stimulation ‘therapy’ and invasive procedures, which carry some health risks. Furthermore, there is a risk of exploitation, in view of the temptation to withhold detailed information on risks for fear of losing ‘willing’ candidate donors (Gerrand, 1993; Gurmankin, 2001). These concerns are, of course, relevant—but they do not justify an absolute ban on creating embryos for research purposes (Warren, 1990; De Wert, 1999). First, the interests of donors may be sufficiently protected by imposing the condition that medical risks should be minimized, by limiting the numbers of hormone treatments as well as the dosage of hormones given to candidate donors. Clearly, a valid consent presumes adequate information about potential residual risks. Second, the creation of embryos for research purposes does not necessarily involve hormonal treatments and/or invasive interventions to get (access to) the oocytes. In clinical IVF/ICSI, it may happen that some oocytes have not yet reached the appropriate stage of nuclear maturity. If they mature further after 24–26 h of in-vitro culture, these oocytes cannot be used clinically, but they may be a good source for making research embryos. Furthermore, in the future, in-vitro maturation (IVM) of oocytes might make hormonal treatments for this purpose obsolete. IVM could even imply the access to new ‘sources’ of research embryos, including aborted female fetuses and cadavers (Human Fertilisation and Embryology Authority, 1994).

A complete prohibition of creating embryos for research purposes would be undesirable. Firstly, a ban would hamper a preclinical risk assessment of new reproductive techniques, such as the cryopreservation and IVM of oocytes. Transferring embryos that have been exposed to (or created by) experimental techniques without adequate preclinical safety studies is morally unjustified as it disregards our duty to minimize the health risks for children thus
conceived (De Wert, 1987; McLaren, 1989; Green, 2001). Secondly, a ban would preclude research into both ‘therapeutic cloning’ and the alternative strategy termed ‘direct reprogramming’ of adult cells, i.e. chemically inducing nuclear reprogramming in the test tube, to derive the required cell type, obviating the necessity for therapeutic cloning altogether (Nuffield Council on Bioethics, 2000; Chief Medical Officer’s Expert Group, 2000; De Wert and Mummery, 2003). The latter option would, if successful, eventually have the dual advantage of both circumventing the creation of preimplantation embryos for instrumental use and the related feminist concerns regarding the autonomy and health interest of women donating oocytes. However, the development of this alternative strategy still requires the production of embryos by nuclear transfer in order to study—and learn how to ‘mimic’—the mechanisms involved in nuclear re-programming.

Multiple pregnancies: prevention or reduction

Multiple pregnancies are the result of either ovulation induction or transfer of several embryos in IVF. Higher order pregnancies are frequently the result of the former. Careful monitoring of the number of ripening follicles via sonogram is recommended, followed by advice to the couple to avoid intercourse or by foregoing insemination if more oocytes are produced. During IVF treatment, replacing several embryos increases the success rate. However, the ‘costs’ of this policy are considerable.

Multiple pregnancies generate a multitude of social, psychological and medical problems for the offspring and the parents, especially the mother. As far as medical risks are concerned, multiple pregnancies are the cause of a strong increase in obstetric complications, perinatal morbidity, congenital malformations and maternal and fetal mortality (Hazekamp et al., 2000; Olivennes, 2000). In addition to these medical risks, the birth of multiples may lead to social and psychological problems. One study showed that 1 year after the birth of triplets, mothers feel socially isolated, overstressed and depressed (Garel and Blondel, 1992). Even 4 years after delivery, mothers of triplets reported fatigue, emotional distress and a difficult relationship with the children (Garel et al., 1997). Mothers of twins also had a significantly higher risk of depression than mothers of singletons (Thorpe et al., 1991). These problems will probably be magnified when one or more children are physically or mentally disabled and when higher-order multiples are involved (Craig, 1999; Elster et al., 2000). Moreover, at a time when the pressure to ration health care is increasing, the extra costs for the care of the children resulting from multiple pregnancies should be taken into account when making the overall balance (Elster et al., 2000). Given the effect of multiple pregnancies on the welfare of all the members of the newly created family, the attitude towards this outcome is a test case for the moral quality of medically assisted reproduction (Pennings, 2000).

Most professional societies have issued guidelines to diminish the percentage of multiple pregnancies after assisted reproduction (British Fertility Society, see Murdoch, 1998; ASRM, 1999; FIGO Committee for the Ethical Aspects of Human Reproduction and Women’s Health, 2000). Still, despite these recommendations for good clinical practice, the percentage of multiple pregnancies remains unacceptably high. The pressure on the IVF centres to maintain a high success rate (in terms of delivery rate) blocks the spontaneous adoption of these rules (Cohen, 1998). There is nevertheless an increasing effort on the part of a number of practitioners to decrease the number of embryos transferred in a given cycle. This strategy was adopted stepwise, going from three embryo transfer to two embryo transfer and finally, at least in a number of centres, to single embryo transfer (Staessen et al., 1993; Gerris and Van Royen, 2000; Dhont, 2001). In some countries, the legislator did not wait for the voluntary adoption of the guidelines and ruled that a maximum of three embryos can be replaced (Bundesrat der Bundesrepublik Deutschland, 1990; Human Fertilisation and Embryology Authority, 2001).

An important ethical issue is who makes the actual decision about the number of embryos transferred. Some physicians consider restrictions on the patients’ wishes as a form of unacceptable paternalism. Several studies have shown that infertility patients do not consider twins and triplets as an undesirable result (Leiblum et al., 1990; Gleicher et al., 1995; Goldfarb et al., 1996; Murdoch, 1997). Still, there are a number of reasons to question the autonomy of patients who seem willing to accept the higher risks of large multiple pregnancies (Murdoch, 1997; De Wert, 1998; Pennings, 2000). The bias caused by the strong desire for a child can be reinforced when financial considerations limit the number of IVF cycles for which the patients can pay (Murdoch, 1998). A recent study showed that women who had a thorough understanding of the specific risks associated with multiple pregnancies were much less desirous of having a twin pregnancy (Groberman et al., 2001). This suggests that most infertile couples were poorly informed about the risks. In general, families are ill-prepared and ill-informed regarding the workload involved in raising multiples. Consistent and extensive counselling of the parents about all dimensions is necessary to avoid unrealistic expectations (Hay et al., 1990).

Another element in the determination of the decision-making authority regarding the number of embryos to be transferred is the causal and intentional contribution of the physician. Since we are talking of iatrogenic problems to which the physician has contributed, he or she inevitably has a professional responsibility for the outcome and remains accountable for his or her collaboration (De Wert, 1998; Pennings, 2000). The physician’s refusal to replace more embryos than he or she considers acceptable need not be seen as a paternalistic intervention for the patients’ good but should rather be considered as the exercise of his or her responsibility for the welfare of the future offspring.

Prevention of multiple pregnancies should be the first goal (American College of Obstetricians and Gynecologists Committee on Ethics, 1999; Nisand and Shenfield, 1997). However, with the present knowledge, it is an illusion to believe that all multiple pregnancies after IVF will be eliminated in the future (Dhont, 2001). Consequently, possible solutions for when the situation presents itself should be considered. Multifetal pregnancy reduction (MFPR) is an acceptable solution when the benefits of reducing the multiple pregnancy exceed the disadvantages of carrying the pregnancy to term and risking miscarriage (Bergh, 1999). Still, this consequentialist reasoning needs to be corroborated by empirical data. The confirmation is especially important when the reduction of triplets to twins or singletons and from twins to singletons is considered. The acceptability of the decision depends largely on the evaluation of the data regarding physical
and mental outcome of triplets and twins. On the one hand, some groups defend the reduction of triplets to twins to improve preterm birth and fetal growth (Vauthier-Brouzes and Lefebvre, 1992; Bollen et al., 1993; Boulot et al., 2000). Increasingly practitioners consider twins as an adverse outcome (Olivennes, 2000; ESHRE Campus Course Report, 2001). If twins are considered as a failure, the reduction of twins to singletons should at least be considered. On the other hand, others concluded that there is no medical indication for the reduction of a triplet pregnancy, let alone a twin pregnancy (Kadhel et al., 1998). The reduction in prematurity, and consequently of the handicaps associated with prematurity, would be fairly restricted (Porreco et al., 1991). Clearly, psychosocial aspects may also be taken into account. Countries in which abortion for serious psychosocial distress is allowed should recognize that the prospect of having twins might constitute a factor of considerable distress for some parents.

It will be difficult to stipulate strong and uniform rules for all patients since the moral significance of a MFPR for both the patient and the physician may be relatively low. They may decide that the increased chance of pregnancy outweighs the burden of this operation. In fact, some physicians explicitly defend the replacement of the number of embryos which maximizes the pregnancy chances of the patient and include MFPR as part of the infertility treatment (Simpson and Carson, 1996). For Simpson and Carson (1996) the acceptance of MFPR by the intentional parents should be a condition for replacing a high number of embryos. Two arguments can be advanced against the adoption of MFPR as part of the procedure (De Wert, 1998). Firstly, for those who attribute an independent moral status and protectability (however limited) to the human fetus, MFPR should be used as a ‘last resort’, i.e. when prevention has failed. Secondly, there remains an increased risk of prematurity and low birth weight for the remaining embryos even after the reduction (Evans et al., 1996; Kanhai, 1998; Evans et al., 2001). Several groups confirmed this residual risk (Alexander et al., 1995; Silver et al., 1997). This implies that the deliberate creation of a multiple pregnancy, even if a reduction is planned, still increases the medical risks for the future children that will be born from the remaining embryos.

The basic moral principle ‘do no harm’ obliges physicians and candidate parents to prevent harm to future offspring as much as is reasonably possible. The ignorance of the professional duty to avoid harm is especially difficult to accept when the cause of the continuing rate of multiplets is found in the competition between centres and physicians for patients and in the financial gains generated by attracting more patients (Faber, 1997; Templet, 2000). However, the avoidance of a multiple pregnancy should not be made into an absolute rule; the main task is to try to find the delicate balance between low pregnancy rates and increased risk of multiple pregnancies.

Sex selection for non-medical reasons by PGD

Sex selection for non-medical reasons is considered unacceptable for large sections of the population. A growing number of countries are preparing or have voted legislation to forbid this application. The Council of Europe stated in Article 14 of the Convention on Human Rights and Biomedicine that ‘the use of techniques of medically assisted procreation shall not be allowed for the purpose of choosing a future child’s sex, except when serious hereditary sex-related disease is to be avoided’ (Council of Europe, 1996). Nevertheless, the discussion re-emerged in recent years due to the development of flow cytometry separation of the X- and Y-bearing sperm. Flow cytometry is the first preconception technique that has proven its efficacy although the selection of females is significantly more effective than the selection of boys (Fugger et al., 1998; Sills et al., 1998). More research needs to be done to demonstrate the safety of the method (Ethics Committee of the ASRM, 2001).

The second development is the use of PGD for social sexing. In the report presented by the ESHRE PGD Consortium for 2001, there appear for the first time data from three clinics regarding gender screening of preimplantation embryos for non-medical reasons (ESHRE PGD Consortium, 2002). The application of PGD for this goal caused great indignation in some members of the consortium, who even opposed the publication of the results (Ray et al., 2002). The Ethics Committee of the ASRM (1999) also considered the application of PGD for sexing for social reasons and concluded that the initiation of IVF with PGD for this reason should be discouraged. When IVF is already done for medical reasons, adding PGD for sexing for social reasons should not be encouraged. Although the Ethics Committee takes a cautious stance towards social sexing in general, it specifically points to the unnecessary medical burdens and costs for parents and to the inappropriate and potentially unfair use of limited medical resources. In a later statement, the president of the Ethics Committee presented the status of the embryo as the main reason for not allowing sex selection for social reasons (Robertson, 2002). The creation and destruction of embryos for this purpose conflicts, according to this statement, with the special respect that is due to fertilized oocytes and preimplantation embryos. The special status of fetuses was also advanced in the debate on the acceptability of prenatal diagnosis followed by abortion as a means for social sexing (Warren, 1990). For others, the lower moral status of preimplantation embryos and the absence of an abortion is sufficient to justify the use of PGD in some circumstances (Pembrey, 2002).

For the proponents of social sexing, the argument that it is unreasonable to have IVF combined with PGD solely to select the gender of the child strongly suggests medical paternalism (Savulescu and Dahl, 2000). The main advantage of PGD in comparison with all preconception techniques is its accuracy (Shushan and Schenker, 1993; Malpani and Malpani, 2002a,b; Steinbock, 2002). However, PGD necessarily suffers from all disadvantages of IVF itself, i.e. it is expensive, invasive and has a limited success rate (life birth/take home baby rate’). The restricted availability indirectly guarantees that most predicted social consequences of a large scale application, for example a skewed sex ratio or a change in the status of women, will not occur (Shushan and Schenker, 1993; Malpani et al., 2002a,b).

For some, the fear that the use of PGD for this reason might discredit the technology as a whole counts as an argument against social sexing (Sills et al., 1999; Pembrey, 2002). For others, the main reason for not permitting sex selection for social reasons is that it can set a precedent for ‘positive eugenics’ applications such as intelligence and athletic phenotype. This danger need not lead to a categorical rejection of social sexing, but urges us to postpone this application until the implications and possible consequences have been thought through (De Wert, 2002). However, for
proponents of social sexing, this type of slippery slope argument (which also refers to the ‘designer babies’) seems overdrawn or invalid (Ethics Committee of the ASRM, 1999; Savulescu, 1999; Pembrey, 2002).

An argument advanced by the opponents of the use of medical techniques, be it sperm sorting or PGD, is that these methods are expensive and are only available to those who can pay for them. This limited access would violate the principle of justice. However, a just health care system only implies universal and equal access to an ‘adequate level’ or a ‘decent minimum’ of health care. Since most people consider sex selection for non-medicinal reasons as an elective health care service that is not part of adequate health care, it should not be reimbursed. Consequently, people who are not able to pay for this elective service are not discriminated against (Pennings, 2002). Allowing the application does not imply subsidising it (McCarthy, 2001).

In the last 10 years, there has been a growing acceptance of sex selection for family balancing. Family balancing is a simple and coherent framework that restricts the application of sex selection. Although it is not a perfect solution for each of the possible problems separately, it simultaneously provides an answer to the birth order problem, the possibility of a skewed sex ratio and the sexism objection (Pennings, 1996). The birth order problem concerns both the unjust advantage of firstborns compared to later siblings and the link of gender with personality characteristics more demonstrated by firstborns. Although these concerns are largely speculative, no such effect can occur since family balancing does not allow the selection of the gender of the first child. Since the concept also implies that only the under-represented sex in the family can be chosen, a distortion of the sex ratio in society is unlikely (i.e. not even if a large number of requests for the technology are made). Finally, the context of family balancing implies that parents do not choose for or against a certain gender but choose for the other gender. Although the context does not guarantee that no sexist motives underlie the parental choice, it minimizes this possibility. Even opponents of gender selection have concluded that ‘there is no intrinsic link between sexism and the desire for a balanced family’ (Wertz and Fletcher, 1989). However, there is no agreement among those who accept sexing within these restrictions regarding the acceptability of the method employed to obtain the goal (Reubinoff and Schenker, 1996; Ethics Committee ASRM, 1999).

A possible compromise would be to allow sex selection for family balancing by means of PGD only when PGD is necessary for medical reasons anyway and no additional testing is needed (Health Council of the Netherlands, 1995). This solution would simultaneously counter the argument that in the present context of rationing health care expenses one should not ‘waste’ an expensive technology. It is clear that, given the moral duty of physicians to give priority to health care needs rather than to elective services of lower importance, the use of PGD for social sexing should not harm those who need the technology to prevent diseases in their children (Pennings, 2002).

Nevertheless, it is important to keep in mind that the distinction medical/non-medical is rather crude. Two intermediate categories should be considered. Firstly, several cases emerging in clinical practice reveal ‘mixed’ indications. HLA typing in order to obtain haematopoietic stem cells for transplantation is an illustration of this category (see below). Another example is the selection of male embryos in case the man has an X-linked recessive disorder like haemophilia A (Santalo et al., 2000). The sons in those cases would not carry the affected gene while all daughters will be carriers. The selection of male, non-carrier embryos would constitute a ‘mixed’ indication: on the one hand, there is no medical reason for performing PGD since female carriers are healthy, while on the other hand, prospective parents may prefer sons because any daughter would be at high risk of having affected sons and, as a consequence, be burdened with complex reproductive decisions (De Wert, 1999). Secondly, a medical indication for sex selection is not necessarily a sufficient justification for sexing. Diseases such as ankylosing spondylitis predominantly affect males and the symptoms are generally more severe in males than in females. The question will undoubtedly arise in the future whether the difference in penetrance and expression of the gene between the sexes justifies sex selection (Pennings, 2002).

**HLA typing of embryos**

The plan to have a child with the intention (and hope) to use it as a ‘donor’ of haematopoietic stem cells for a sibling has been executed for years with the means available at that time. Before the possibility of prenatal HLA typing, parents decided to have another child, hoping that it would be a match (Burgio et al., 1987; Burgio et al., 1997). In the next phase, parents conceived and planned to verify the suitability of the fetus as a donor prenatally. A survey carried out by Kearney and Caplan (1992) revealed that several cases were known where parents were prepared to abort if the fetus was not a match (Clark et al., 1989; Norton, 1994). The last step in the evolution is the application of PGD. In this case, PGD is used to select an embryo with an HLA type that is matched to that of a sick sibling in need of a transplantation of haematopoietic stem cells. The main advantages of this procedure compared with the other methods are the possibility of avoiding recurrent abortions (and thus the reduction of the burden on the woman), the availability of a large number of embryos from which to choose and, consequently, a much greater chance of finding an HLA-matched embryo within the shortest possible time period (Verlinsky et al., 2001; Pennings et al., 2002). Moreover, if the recipient sibling weighs <40 kg, umbilical cord blood can be used, thus avoiding the need for an invasive intervention in the donor. Still, aggressive early cord clamping may deprive the donor of placental blood which might harm a premature or very low birth weight newborn (American Academy of Pediatrics, 1999). The first application of HLA typing by means of PGD was performed for a child with Fanconi anaemia (Verlinsky et al., 2000).

In most cases, the HLA typing will be performed in addition to the diagnosis for the genetic disease that affects the sick sibling. However, the use of this procedure could also be justified for couples without a family history of genetic disease (Boyle and Savulescu, 2001). Although HLA typing does not fit into the medical model for prenatal and preimplantation diagnosis (since the HLA type is not relevant for the future child itself), it clearly serves the health interest of the sibling (De Wert, 2002; Pennings et al., 2002). This benefit is sufficient as a justification in itself, even without the wish of preventing the disease in future offspring. Perhaps a concept such as IVF/PGD with ‘therapeutic intent’ could help us out here (Wagner, 2001).
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A common ethical argument advanced against this kind of request is the instrumentalization of the child. The future child would be used as an instrument to cure another child. Most opponents refer to the famous Kantian categorical imperative which says that one ‘should act in such a way that you always treat humanity, whether in your own person or the person of any other, never simply as a means, but always at the same time as an end’ (Kant, 1964). It is not easy to decide in practice when someone is used as an instrument (Drebushenko, 1991). Moreover, Kant’s crucial point lies in the rejection of using a person solely as a means (Jecker, 1990; Splett, 1990; Zucker, 1992). Only two actions by the parents would demonstrate such an attitude: the abuse and neglect of the donor child and the surrender of the child for adoption after taking the tissue. Although it could be argued that the child given up for adoption is not harmed by this decision (Robertson, 1994), it would certainly be wronged. Most importantly, however, there are no indications at present that parents who ask medical assistance to obtain an HLA-compatible sibling do not intend to love and care for the donor child to the same extent as they do for their other children.

In connection to the former objection, one frequently refers to this application as the first step on the slippery slope towards ‘designer babies’. According to the designer model, parents are allowed to choose specific features of their future child which do not benefit the child itself. However, this argument ignores the ‘therapeutic intent’ mentioned above. Furthermore, it should be realised that parents opting for the current strategy are not designing their ideal prospective child (intelligent, athletic, etc.)—they just want to have a normal child, and to use the haematopoietic stem cells to save another child.

Another argument against the conception of a child to save a sibling is the possible experience of the donor child. This argument seems to be little else than a reformulation of the moral position one adopts on this issue. Those who oppose this application predict that the child will feel used and devalued. However, without empirical data, one can just as easily predict that the child will feel proud to have saved the life of a sibling (Thomasma, 1992). In the exceptional case where there has been a follow-up of the siblings, the psychosocial relationship developed normally (Burgio et al., 1997). Moreover, the proposal to ‘hold back until more is understood of the risks of psychosocial maladjustment’ (Editorial, 2001) is not useful since the only way to find out whether there is such risk is by the follow-up of the children. This presupposes that the technology is at least temporarily accepted.

On the other hand, enthusiasm should not blind us to the possible pitfalls and uncertainties of such applications. The application of this technology should be accompanied by extensive counselling during which the counsellor verifies, as far as this is reasonably possible, the real intention and the capacity of the parents to accept the child into their family as an equal member. In addition, the following risks and pitfalls should be explicitly considered during counselling: the possibility that no matching embryos are found or that no pregnancy occurs, the possibility that the transplantation fails or that the recipient child dies before the transplantation. Given the accumulation of probabilities in the different steps of the procedure, one should seriously consider the acceptability of this solution in the light of the final chance of success. Even if the final chance of a successful transplantation is relatively small, the possible benefit for both the sick sibling and the family is substantial. HLA typing of the embryos by means of PGD should not be presented as an easy and guaranteed solution for the parents’ problem (De Wort, 2002). It should be evaluated on a case-by-case basis whether the procedure, everything considered, is the best solution for this family.

As a form of prospective ethics, we should anticipate new requests on at least two dimensions, i.e. tissue type and beneficiary. According to a newspaper article, the first request has been entered in the UK where the recipient is not a sibling but the father of the future child suffering from thalassaemia (Brown and McKie, 2000). The Australian Infertility Treatment Authority (2002) restricts the application to cases where the intended tissue recipient is a sibling. Regrettably, no argument is offered for this clause. It is not self-evident that a non-sibling recipient alters the moral evaluation of the request. The second dimension on which the applications may alter is the type of tissue needed. Both the HFEA and the Infertility Treatment Authority restrict the application to the provision of cord blood and bone marrow (Ethics Committee of the HFEA, 2001; Infertility Treatment Authority, 2002).

In summary, the conception of a child as a future donor for a sibling does not necessarily show a lack of respect for that child and neither does it infringe the child’s autonomy (Jecker, 1990). In view of the possible pitfalls and uncertainties, adequate counselling is a conditio sine qua non.

References


