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DEBATE

Extending preimplantation genetic diagnosis: the ethical debate

Ethical issues in new uses of preimplantation genetic diagnosis

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The use of preimplantation genetic diagnosis (PGD) to screen embryos for aneuploidy and genetic disease is growing. New uses of PGD have been reported in the past year for screening embryos for susceptibility to cancer, for late-onset diseases, for HLA-matching for existing children, and for gender. These extensions have raised questions about their ethical acceptability and the adequacy of regulatory structures to review new uses. This article describes current and likely future uses of PGD, and then analyses the ethical issues posed by new uses of PGD to screen embryos for susceptibility and late-onset conditions, for HLA-matching for tissue donation to an existing child, and for gender selection. It also addresses ethical issues that would arise in more speculative scenarios of selecting embryos for hearing ability or sexual orientation. The article concludes that except for sex selection of the first child, most current extensions of PGD are ethically acceptable, and provides a framework for evaluating future extensions for nonmedical purposes that are still speculative.

Key words: embryo screening/ethics/gender selection/HLA matching/preimplantation genetic diagnosis

Introduction

Debate about new genetic and reproductive technologies has often cited preimplantation genetic diagnosis (PGD)—the technique by which early human embryos are genetically screened and then discarded or placed in the uterus—as a reproductive practice that needs close ethical, legal, and social scrutiny. Reports that embryos are being screened for new indications such as susceptibility conditions, late-onset diseases, HLA matching for existing children, and gender, reinforce the need for greater public attention. The purpose of this article is to describe current and likely future uses of PGD, and analyse the ethical, legal, and policy issues which they pose.

State of the art

PGD has been available since 1990 for testing of aneuploidy in low prognosis infertility patients, and for single gene and X-linked diseases in at-risk couples. A report in July, 2001 on worldwide use of PGD since 1990 reported that embryo or polar body biopsy has occurred in more than 3000 clinical cycles, with a 24% pregnancy rate, which is comparable with assisted reproductive practices which do not involve biopsy (Conference Report, 2001). More than 1000 children have now been born after PGD, and many pregnancies are ongoing (Tanner, 2002). The available data also indicates a 97% accuracy rate in preimplantation diagnosis, despite a high rate of allelic drop-out in single cell PCR and the possibility of mosaicism or chaos in tested embryos.

Although some 40 centres worldwide have done PGD, four centres (Chicago, St Barnabas, Bologna, and Brussels) accounted for 2774 of the 3000 reported PGD cycles, and had an overall 29% clinical pregnancy rate (Conference Report, 2001). All four centres have done most of their PGD for aneuploidy, but Brussels has also concentrated on single gene analysis of blastomeres, and Chicago on polar body analysis. Other centres in the United States and Western Europe also do PGD, including four centres in London and centres in the Eastern Mediterranean, in Southeast Asia, and in Australia. While expansion in the number of centres offering PGD is to be expected, the investment of time, skill, and equipment needed for a competent programme may limit the number of IVF programmes providing this procedure. More work assessing the science, safety, and efficacy of PGD is needed as the field develops.

The demand for PGD

Although the use of PGD will grow, only a small number of people using assisted reproduction, and thus a much smaller of people overall who reproduce, are likely to use PGD to screen embryos. One reason is that accessing embryos through IVF is intrusive and expensive, and for some people raises serious ethical concerns. Thus patients will only seek it if there is a sufficient reason for them to do so, and insurance coverage and access to PGD facilities is provided.

PGD is least burdensome for a couple already going through IVF for infertility due to advanced maternal age. The additional

costs of embryo biopsy and karyotyping could be justified if they produce a marked improvement in pregnancy rates. Non-IVF patients, however, would seek PGD only if they were at special risk for genetic disease, and wanted to have a child without risking an affected pregnancy or later abortion. In both cases prenatal diagnosis would still be done to confirm that a fetus does not have the condition that the couple is seeking to avoid.

Several new indications for PGD single gene mutational analysis have been reported. These indications should increase demand for PGD from some couples unwilling to use prenatal diagnosis and selective abortion for those conditions. New uses include PGD to detect mutations for susceptibility to cancer and for late-onset disorders such as Alzheimer's diseases. In addition, parents with children needing haematopoietic stem-cell transplants have also used PGD to ensure that their next child is free of disease and is a good tissue match for an existing child. Some people are also requesting PGD for gender selection for both first and later born children.

The emergence of new uses for PGD have made PGD a frequent target of ethical commentary and speculation about a future of greatly increased genetic selection and manipulation of offspring (Fukuyama, 2002; Kass, 2002; Stock, 2002). However, the low penetration of PGD in reproductive practice is likely to continue for some time. Even if PGD becomes the standard of care for older IVF patients, it is unlikely because of cost and lack of need to spread to good prognosis patients. Its use for screening for susceptibility and late-onset diseases is limited by the few diseases for which single gene predispositions are known. In addition, relatively few parents will face the awful dilemma of a sick child in need of a haematopoietic stem-cell donor, that might lead them to consider PGD. Gender preferences in offspring, however, might lead to demand for PGD in some cultural contexts. In short, PGD is likely to be increasingly sought by patients in narrow risk groups and to some extent for sex selection, but that demand will remain a small percentage of people using assisted reproductive and prenatal services. Despite the relatively limited use of PGD, the ethical, legal, and policy issues that arise from these new uses require attention.

Ethical issues in current and expanded uses of PGD

Two main sets of ethical objections make PGD and proposals for its extension controversial. One set of objections arises from the need to create and then select embryos on chromosomal or genetic grounds, with the deselected embryos then usually discarded. Other objections concern the fact of selection itself.

Objections to PGD based on its effect on embryos replay debates over abortion and embryo status that have occurred in many other contexts, from abortion to embryonic stem cell research. People who think that the embryo or fetus is a person will object to creating and destroying embryos, and oppose most uses of PGD. Others believe that preimplantation embryos are too rudimentary in development to have interests or rights, but that they deserve special respect as the first stage toward a new person (American Society of Reproductive Medicine, 1994). Under this view PGD is ethically acceptable when done for good reasons, such as preventing offspring with serious genetic disease. Indeed, PGD may prevent selective abortions for those diseases. A major issue with new uses of PGD is whether they sufficiently benefit important human interests to meet the demands of special respect for embryos that supporters of PGD may require.

A second set of objections arises from the fact of selection itself, and the risks of greatly expanded future selection of embryos and children. Sometimes based on religious views about the nature of human reproduction, ethical objections to selecting offspring traits raises two kinds of ethical concerns. One kind is deontological—the ethical judgement that it is wrong to choose traits of offspring, no matter how well intentioned. Dr Leon Kass has articulated this view, as has the President's Bioethics Council in the United States, which he chairs. They argue that human reproduction is a 'gift' and that any form of selection or manipulation turns the child into a 'manufacture' and thus impairs human flourishing (Kass, 1998, 2000, 2002; President's Bioethics Council, 2002). The second kind of concern is consequentialist. It arises from fears that increasing the frequency and scope of genetic screening of prospective children will move us toward a eugenic world in which children are valued more for their genotype than for their inherent characteristics, eventually ushering in a world of 'designer' children in which genetic engineering of offspring becomes routine.

While recognizing the strong objections of some people to PGD on these grounds, the following discussion assumes that the use of PGD to screen for aneuploidy and serious Mendelian disorders is ethically and legally acceptable when performed according to applicable regulatory guidelines. It concentrates instead on new indications for PGD, and asks whether they would also meet ethical standards of acceptability.

Expanded uses of PGD in assisted reproduction

The most common use of PGD is to screen embryos in assisted reproduction for chromosomal abnormalities before transfer. At present there is no reliable way to assess the viability of in-vitro embryos other than by visual examination of morphology, but that method is not reliable, especially in low prognosis patients >39 years of age.

Testing for aneuploidy is now limited by the practice of examining only a few chromosomes. Some centres are now introducing full karyotyping of single blastomeres or polar bodies, which could improve accuracy in selecting viable embryos for transfer. A much greater use of PGD for low prognosis patients may be expected. Indeed, some practitioners have suggested that aneuploidy analysis for this group may soon become the standard of care, though overall efficacy has not yet clearly been established (Conference Report, 2001).

PGD is also useful for couples with chromosomal translocations who have experienced repeated spontaneous abortion. Robertsonian translocations, for example, may occur as frequently as 1 in 1000 in many populations. Centres in New Jersey, Chicago, and London (Guy's & St. Thomas') have developed methods of identifying unbalanced translocations

that enable couples with a history of spontaneous abortion or other problems to have children (Conference Report, 2001; Scriven *et al*., 2001).

The use of PGD to exclude aneuploid embryos from transfer raises few special ethical issues beyond the use of IVF itself and discard of embryos. Nontransfer of embryos on visual grounds is now standard practice, so improving the grounds for selection is a gain. Nor does karyotyping for aneuploidies or translocations affecting fetal viability implicate ethical concerns about selecting embryos on nonmedical grounds. Ethical problems could arise, however, if programmes unequipped to do these procedures offer them to patients. Careful patient selection is also important, for PGD is not always indicated, even for patients with genetic anomalies (Scriven *et al*., 2001). Consultation with institutional ethics and research committees is essential before a programme begins to offer PGD services.

PGD for Mendelian diseases

In addition to full or partial karyotyping of chromosomes, PGD also allows direct examination of specific sections of the genome for mutations. Close to 1000 PGD cycles have been done for single gene disorders, resulting in at least 200 clinical pregnancies and 130 children born to date. More than half of these were done by the Brussels and Chicago centres, with Brussels specializing in blastomere biopsy and Chicago in polar body analysis. (Conference Report, 2001). Mutational analysis requires additional skills beyond karyotyping, including the ability to conduct multiplex PCR with nested primers of the gene of interest and related markers.

PGD from its inception has been touted as an important alternative for couples who were carriers of autosomal recessive, dominant, or sex-linked diseases such as Tay Sachs, cystic fibrosis, sickle cell anaemia, Duchenne muscular dystrophy, and haemophilia. Rather than take a chance that a child would be born affected, some couples would go childless, adopt, or use donor gametes. Some at-risk couples have conceived and then undergone prenatal testing. If the result was positive, they then had the option of terminating the pregnancy, a difficult and burdensome decision.

PGD offers the alternative of screening embryos rather than fetuses, thus avoiding the need to terminate a pregnancy in order to ensure an unaffected child. A couple selecting this approach would have to forego coital conception and undergo the costs and rigours of IVF, but may have a higher chance of successful pregnancy than would most infertile couples using IVF. Chorion villus sampling or amniocentesis later in the pregnancy is still advised to confirm the negative diagnosis.

PGD to screen out embryos affected by Tay Sachs, sickle cell, cystic fibrosis or other serious diseases raises no ethical issues beyond those that arise with prenatal diagnosis and selective termination of pregnancy generally. Many at-risk couples might find embryo selection preferable to pregnancy termination because of the undeveloped state of embryos compared with fetuses. Unless PGD were available, some at-risk couples might forego reproduction rather than risk an affected child or terminating an affected pregnancy.

PGD for susceptibility conditions

A logical extension of PGD for Mendelian disorders is its use to avoid the birth of children who are healthy at birth but face a higher than average risk of having cancer or some other serious disease. Indeed, PGD has been carried out to avoid the birth of a child with *P53* mutations—in this case the Li-Fraumeni syndrome (Simpson, 2001; Verlinsky *et al*, 2001a), and may be sought for *BRCA1* and *2* susceptibility for breast cancer. Ethically, the question is whether the burdens of carrying susceptibility genes is so great for the child and parents that the burdens of IVF and PGD to screen embryos to avoid the affected children are justified. Many couples with these conditions might choose to go childless, rather than subject their child to the monitoring and worries that having known susceptibility genes carry. PGD may now make it possible to establish pregnancies free of the feared susceptibility condition.

The arguments in favour of such a use are similar to the arguments for avoiding the birth of children with a serious autosomal or X-linked condition. Parents have a strong, interest in having children who will be healthy and not face the burdens of continued monitoring, prophylactic surgery, or other preventive actions, none of which is guaranteed to prevent the disease. If one accepts that embryos lack rights and interests but deserve special respect, then a plausible case for permitting PGD for this purpose exists. Creating and destroying embryos to have a healthy child does not treat embryos in a cavalier or frivolous way, and thus is consistent with special respect due embryos. The fact that the disease state does not occur until much later in life, unlike other Mendelian disorders, should not be morally significant. Having a child with inherited susceptibility to cancer could be a major source of suffering for parents and child, and could well affect a parental decision to reproduce (Simpson, 2001).

PGD for susceptibility conditions is legal in the United States. The Human Fertilisation and Embryology Authority (HFEA) in the UK has not yet granted licences for PGD for susceptibility testing. But it would fit within the statutory framework and should be permitted when application is made.

The chief legal restriction on susceptibility testing at present may come from people holding patents on the genes tested for by PGD. Myriad Corp., which holds the patent on the *BRCA1* and *2* genes, requires that all tests be done on samples shipped to Utah, and refuses to offer the test for reproductive purposes (Myriad Policy Brochure, 1998). If their patents are valid and are enforced, women with breast cancer genes may not be able to use PGD to screen out daughters with those mutations. But this is an artefact of patent law, which gives patent holders the right to stop even highly beneficial uses of their inventions, not the ethics of PGD. A challenge to the Myriad patents, now before the European Patent Office, could, if successful, increase access to BRCA gene testing by PGD in Europe.

PGD for late-onset conditions

PGD has also been used by a woman who carried a gene for early onset Alzheimer's disease (AD), and who wished to have a child that would be free of that condition. In that case the woman was 31 years of age, had an older sister who had

already experienced early onset Alzheimer's, and had herself tested positive. She requested PGD to be sure that any fetus that she carried did not also have that gene. PGD was carried out, and she gave birth to a child free of that condition (Verlinsky *et al*., 2002).

The ethical issues raised here are similar to those raised for susceptibility conditions with one additional feature. As in those cases, avoidance of a child who will be healthy for a number of years but then in her 30's or 40's will experience AD [or Huntington's disease (HD)] is a substantial, non-trivial reason for employing PGD, as weighty as its use to avoid a child with susceptibility or disease genes. Indeed, the case is even stronger because the diseases tested for are not preventable, as may be the case with susceptibility genes.

The ethical twist in this case, however, concerns the ability of the affected parent to raise the child. Because late onset conditions like AD and HD are dominant, people would not be tested unless they knew that they carry (or are at risk of carrying) the disease gene themselves and faced a greatly shortened life span. Despite this knowledge, they wish to have offspring, but only if they can be sure that their child will not also have the disease. But having a child free of the disease means that that child is likely to lose a parent to the disease while still dependent on them.

The ethical issue is whether physicians act properly when they enable a woman/couple to have a child knowing that the child may soon lose one parent. Some ethicists have questioned whether helping to have a child when the parent may die prematurely is a responsible act, and some physicians or programmes may refuse to offer such services (Towner and Loewy, 2002). Yet a plausible case exists that such actions are ethical. People in this situation have as strong an interest in reproduction as other people receiving infertility services. The fact of a shortened life span makes reproduction for that person all the more acute and pressing, and is the only chance for her partner to reproduce with her. To be consistent, denying reproductive services in this case would also require denying sperm preparation and intrauterine insemination when an individual or her partner has HIV, providing IVF to a woman in her 30's with cystic fibrosis, or initiating a pregnancy with a cancer patient's gametes or embryos that were stored prior to radiation or chemotherapy.

It is true in all these cases that the child faces, with varying degrees of risk, having one of her parents die earlier than generally occurs, and will suffer grief and loss as a result, but another parent or care-giver is almost certain to be present. In addition, the child in question could not otherwise be born but with this risk. The psychological trauma of dealing with the death or illness of a parent does not make a life so full of suffering or without clear benefit that one is harming the child by enabling her birth. As a result, one cannot persuasively condemn parents (and the physicians who help them) who reproduce in those circumstances as causing unnecessary or undue suffering for their children.

PGD for HLA matching for an existing child

PGD has also been used to enable a family with a child with Fanconi anaemia to have another child who would serve as a source of haematopoietic stem cells obtained from that child's umbilical cord blood (Verlinsky, 2001b). Without a stem cell transplant, the first child is likely to die. Non-sibling matches, even if available, are not nearly as safe and effective as sibling donations. If no sibling exists, parents might conceive coitally and hope to have a child who is a suitable match. Although rare, some parents might undergo prenatal diagnosis and abort if the fetus is not a good match, or even carry the fetus to term and give up the child for adoption (Auerbach, 1994).

Parents willing to have another child to produce stem cells for an existing child will find PGD attractive because it enables them to transfer to the uterus only embryos free of the disease and HLA-matched to the existing child. The situation differs from other situations discussed because the PGD is done wholly or in part to choose embryos that will enable the resulting child to serve as an HLA-matched donor for an existing child. Yet this distinction should not matter morally (Pennings *et al*., 2002; Robertson *et al*., 2002). Although helping an existing child is a motivating factor in having an additional child, such a reason alone is not likely to make the parents ignore the needs of the new child. With stem cells available from umbilical cord blood no further intrusions on the new child will occur. Its birth might save the life of an existing, loved child, which would only increase its specialness. If the stem cell transplant fails, the parents will have a surviving child to love. Creating and discarding embryos to provide donor cells for an existing child is not a trivial or frivolous use of embryos, and thus is consistent with the special respect that the nonright-to-life position accords to human embryos.

The HFEA has found PGD for HLA matching to be acceptable where the children born after PGD were themselves at risk for the condition to be treated in the existing child (Human Fertilisation and Embryology Authority, 2002). This means that it would be acceptable to use PGD for HLA matching in cases of Fanconi's anaemia, but not childhood leukaemia or lymphoma unconnected to a known genetic mutation that later children might inherit. This limitation might be a prudent step to ensure that expanded uses of PGD occur slowly, but may not be entirely justifiable in terms of the principles that underlie allowing PGD for Mendelian disorders or other conditions. Whether or not the embryo itself is at risk for the disease for which stem cells are sought, screening for closeness of HLA match for an existing sick child serves a substantial family need and is not abusive or commodifying of resulting children (Robertson *et al*., 2002). The HFEA limitation should be reconsidered, and should not be followed in other jurisdictions (facing the issue).

PGD for gender selection

A controversial use of PGD is for nonmedical sex selection—to serve parental interests in having a healthy child of a particular gender. Because PGD for gender selection requires karyotyping only the sex chromosomes, it is more easily done than karyotyping for other aneuploidies or than single gene mutational analysis.

Requests for PGD for gender selection have come from two different groups. One is from people who wish to select the sex of their first born child. In almost all cases the first-born

preference is for a male child due to cultural mores that prefer males to perform certain rituals or to carry on the family line, or from rank sexism (Robertson, 2001). The second group is from people who already have a child of one gender and wish to have a child of the opposite gender. In many cases those requests are made after a family has had two or more children of the same gender, with no greater preference for males than for females.

In either case PGD for nonmedical gender selection is highly controversial, because gender selection itself seems to be a less compelling reason for selection of embryos for transfer. If sex selection for first children were carried out on a large scale, it could lead to great disparities in the sex ratio of the population, as has occurred in China and India (Sen, 1990; Eckholm, 2002). Since PGD is unlikely to be widely practised, however, its use for the first child is only marginally likely to contribute to those disparities. However, its use for first children is likely to reflect culturally-founded sexist notions. As middle and upper classes in those cultures expand and have the means to obtain PGD, such demand could grow.

The use of PGD to select the sex of second or subsequent children is much less susceptible to a charge of sexism if used to choose a gender opposite to that of an existing child or children. Here a couple seeks variety or 'balance' in the gender of offspring because of the different rearing experiences that come with rearing children of different genders. Psychologists now recognize many biologically-based differences between male and female children, including different patterns of aggression, learning, and spatial recognition, as well as hormonal differences (Robertson, 2001). It may not be *per se* sexist to wish to have a child or children of each gender, particularly if one has two or more children of the same sex.

Some feminists, however, would argue that any attention to the gender of offspring is inherently sexist, particularly when social attitudes and expectations play such an important role in constructing sex role expectations and behaviours. Other feminists find the choice of a child with a gender different from existing children to be morally defensible as long as ''the intention and consequences of the practice are not sexist'' (Mahowald, 2000). As United States Supreme Court Justice and former feminist lawyer Ruth Bader Ginsburg noted in an important sex discrimination case, ''the two sexes are not fungible... inherent differences between men and women, we have come to appreciate, remain cause for celebration'' (United States Supreme Court, 1996). Desiring the different rearing experiences that one has with boys and girls does not mean that the parents, who have already had children of one sex, are sexists or likely to devalue one or the other sex (American Society of Reproductive Medicine, 2001).

Based on this analysis the case is not strong for allowing PGD for the first child, but may be acceptable for gender variety in a family. With regard to the first child, one may be promoting or entrenching sexist social mores. One could also argue that creating embryos to choose the gender of the first child is not a strong enough reason to show special respect for embryos. A proponent of sex selection, however, might argue that in certain cultures having a first-born male is so important that it is a legitimate reason for creating and destroying embryos. If PGD is not permitted, pregnancy and abortion might occur instead.

The case for PGD for gender variety is stronger because the risk of sexism is lessened. A couple would be selecting the sex of a second or subsequent children for variety in rearing experiences, and not out of a belief that one sex is privileged over another. Sex selection in that case would occur without running the risks of entrenching sexism and hurting women (American Society of Reproductive Medicine, 2001). But is the desire for gender variety in children, even if not inherently sexist, a strong enough reason to justify creating and discarding embryos on that basis? The answer depends on how strong an interest that is. Aside from anecdotal evidence, it is unclear how many parents are in that situation and how strong the desire for gender variety is. If it is a strong one, e.g., would stop parents from having another child unless they could be certain it would be of the sex opposite of existing children, then perhaps it should be acceptable as well. However, more evidence of the strength of the need would help in reaching a final conclusion (Robertson, 2002).

It is instructive to see how the American Society of Reproductive Medicine (ASRM), a leading American organization of fertility doctors, has dealt with this question. The Ethics Committee of the ASRM initially addressed the issue of PGD for sex selection generally, and found that it ''should be discouraged'' for couples not going through IVF, and ''not encouraged'' for couples who were, but made no distinction between PGD for selecting the sex of first and subsequent children (American Society of Reproductive Medicine, 1999). Subsequently, it found that preconception gender selection would be acceptable for purposes of gender variety but not for the first child (American Society of Reproductive Medicine, 2001).

Perceiving these two positions to be inconsistent, a doctor who wanted to offer PGD for sex selection inquired of the Ethics Committee why preconception methods for gender variety, which lacked 100% certainty, were acceptable but PGD, which guaranteed that certainty, was not. Focusing only on the sexism and gender discrimination issue, the Chair of the Ethics Committee, in a widely publicized letter, found that PGD for gender balancing would be acceptable (Kolata, 2001). When the full committee considered the matter, it concluded that it had not yet received enough evidence that the need for gender variety was so important in families that it justified creating and destroying embryos for that purpose (Robertson, 2002). In the future if such evidence was forthcoming then PGD for gender variety might also be acceptable.

What might constitute such evidence? One source would be families with two or more children of one sex who would have another child only if they could be sure that it would be a child of the sex opposite of existing children. Given the legitimacy of wanting to raise children of both genders, reasonable people might find that this need outweighs the symbolic costs of creating and destroying embryos for that purpose. Selection in that case could enable a couple to have a child that they would not otherwise have had, a goal served in other cases of embryo screening. A variation on this need might come from families that had suffered the death of a child and wanted to have

another child of that sex. Still another variation has arisen in Israel, where the Ministry of Health has approved use of PGD to select a girl for a couple using an anonymous sperm-donor, to prevent the disclosure of the male infertility that would likely occur if the child were male (Traubman and Shadmi, 2002).

Another arguably acceptable use of PGD for gender variety has been reported in India, where an IVF programme in Bombay is now providing PGD to select male offspring as the second child of couples who have already had a daughter (Malpani *et al*., 2002). Because of the importance of a male heir in India, those couples might have resorted to abortion if pregnant with a female fetus (even though illegal for that purpose). In that setting PGD for sex selection for gender variety appears to be justified.

PGD for nonmedical traits

Other controversial uses of PGD would arise if genetic tests for nonmedical traits such as hearing, sexual orientation, height, beauty, intelligence, or other factors became available (Kass, 1998; Fukuyama, 2002; Stock, 2002). Untangling the inherited basis of phenotypic traits strongly influenced by learning and environment will not be simple, and such tests, with a few exceptions, are unlikely to be available, if at all, for some time to come.

One potential would be tests for GJB2 mutations, which are the largest known contributor to inherited deafness (Nance and Pandya, 2002). If such a test is available, people with a family history of deafness might request PGD to screen out embryos with the mutation, in order to increase their chances of having a hearing child. Because hearing is clearly beneficial to a child, a major ethical concern with this practice would be the prejudice to the deaf community that it might cause. For such screening to be acceptable, it is essential that it not be offered in ways that denigrated the deaf or lessened respect for them.

The reverse situation—a deaf couple wants PGD to screen out embryos that do not have the GJB2 mutations—could also arise. Here the ethical issue is whether having a deaf instead of a hearing child would have hurt that child. A similar issue has arisen in a widely publicized case of a deaf lesbian couple choosing a deaf sperm-donor in order to increase the chances of having a deaf child. Given the deaf parents' strong commitment to the well-being of their child and the rich culture now available to deaf people, many bioethicists analysing this case find the deaf parents' choice to be acceptable (Davis, 2001; Fletcher 2002; Levy, 2002). Others, however, strongly disagree (Anstey, 2002).

Similar issues would arise if a genetic test for sexual orientation became available. A main ethical concern would be whether use of the test to avoid offspring with homosexual orientation would increase discrimination or antipathy toward gays. The concern with using the test to ensure a homosexual orientation in one's child is whether this shows a responsible regard for the well being of the child. Much would depend on the precise circumstances of use and the characteristics of people seeking the test.

Some people would strongly urge that selection for hearing ability, sexual orientation, or other traits should never be permissible (Fukuyama, 2002; Kass, 2002). Reinforcing their concern is the fear that such uses of PGD will inevitably lead to more drastic efforts at selection and alteration of offspring traits. Although PGD acts negatively by screening out embryos, it accepts the principle that parents might rightfully exercise control over the genomes of offspring. It will then be much easier to take the next steps leading to positive alteration and engineering of offspring traits and the risk of 'designer' children which that will bring.

Although it is useful to identify the ethical issues that such uses would potentially raise, it is too soon to reach definitive judgements about whether these uses, if ever feasible, would or should be permitted. Such tests are too far off in the future to make informed judgements about them now. Until they are closer to practical reality, they should not be an important factor in determining the acceptability of more feasible uses.

Making public policy for PGD

Legitimate concerns about potential misuse of embryo screening and selection make it essential that a sustained public debate about these issues occurs as technical progress continues. Some of the discomfort that surrounds new uses of PGD stems from a sense in many countries that there is no effective oversight of its development and use.

The case is different in the UK, where the HFEA has legal authority over whether a clinic is licensed to do PGD at all and for what indications. Additional uses of PGD may occur only if the HFEA is satisfied that the uses are within statutory guidelines and the programme is qualified to undertake the work. In addition, the HFEA uses a public consultation process to assess public attitudes and draw up guidelines for new uses, as demonstrated in its consultation process for whether PGD was acceptable for HLA matching of embryos with existing sick children (Human Fertilisation and Embryology Authority, 2002). While some physicians have challenged the scope of the HFEA's regulatory authority, the HFEA has provided a regulatory model that other nations might emulate.

The situation in the United States is quite different. No agency exists at the state or federal level that plays a role comparable with that of the HFEA. Congress exercises some control by refusing to fund research or use of PGD, but this often means that the activity escapes meaningful external review in the private sector. A few States have laws restricting embryo research, but several of them have been struck down as unconstitutionally vague or intrusive on reproductive rights, and the others are vulnerable to the same charges. State malpractice and tort law will apply, but those restrictions provide little oversight of the ethical acceptability of new procedures. How PGD is used and for what indications is thus left largely to the discretion of providers offering those services and the patients who seek it.

Even if there is no HFEA-like authority for public oversight, extensive public debate is desirable as new techniques become available. With PGD, the need for a new agency or more explicit public controls may be less pressing than initially thought. As this article has discussed, most of the new uses of PGD now under consideration fit easily into old categories of efforts to ensure that offspring are healthy. More controversial

uses, such as for gender selection, are not as readily accepted and practised, though some increase of PGD for gender selection, especially for gender variety, is likely. Except for deafness and possibly sexual orientation, using PGD to select for other nonmedical traits, if ever possible, is too far off in the future to justify final judgements about them now.

Conclusion

PGD is increasingly available for aneuploidy in low prognosis IVF patients and for single gene mutations that cause genetic disease, susceptibility to cancer, and late onset disorders. If PGD is acceptable to prevent offspring with serious genetic disease, then these additional uses should be acceptable as well. There is also ethical support for using PGD to assure that a child is an HLA match with an existing child. More controversial is the use of PGD for gender selection, particularly for the first child. Equally controversial would be its use to screen embryos for hearing, sexual orientation, and other nonmedical traits—uses that are now highly speculative. Careful ethical analysis and open public debate is essential if new uses of PGD are to become acceptable methods for having children.

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