

Ethics and the future of preimplantation genetic diagnosis



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Abstract

The future growth of preimplantation genetic diagnosis (PGD) will depend on refinements in genetic knowledge and genetic analysis of blastomeres. Equally important, however, is an acceptance of the ethical legitimacy of parents using technologies to select genetic traits of offspring. Objections based on embryo status, the giftedness of reproduction, eugenics, and protecting the child's welfare are not convincing grounds to oppose most uses of PGD. Whether PGD should be accepted for new medical or non-medical uses should depend upon a careful assessment of the proposed use's importance to the person or couple requesting it, and the harmful effects, if any, which it might cause. Such an approach leads to the conclusion that most new medical uses of PGD and some non-medical uses should be permitted.

Keywords: embryos, deafness, eugenics, preimplantation genetic diagnosis, regulation, sex selection

Introduction

The use of preimplantation genetic diagnosis (PGD) is rapidly growing and in coming years is likely to continue to grow. PGD is now used primarily for aneuploidy screening, to identify chromosomal translocations, and to avoid the transfer of embryos with autosomal and X-linked Mendelian early onset diseases (International Working Group on Preimplantation Genetics, 2001). In addition, some persons seek PGD in order to have an HLA-matched child to provide haematopoietic stem cells for an existing child and for non-medical gender selection. Some commentators predict that PGD will eventually be used to screen for other non-medical traits as well.

This paper discusses technical and ethical factors that will affect future applications of the technique, and provides a methodology for resolving ethical conflicts about new indications for PGD. It then illustrates that methodology by examining one medical and two non-medical extensions of PGD.

Technical and economic factors

The scope of future application of PGD depends on many factors both technical and ethical. Unless the technique works safely and effectively at a reasonable cost, it will play but a

small role in the reproductive plans of most individuals. The IVF on which it depends must be safe, effective, and within the financial means of persons who would benefit from it. In addition, the personnel and resources for highly accurate PGD must also be available. While many IVF clinics are equipped to remove the individual cells needed for chromosomal or genetic analysis, fewer of them will have the expertise to do chromosomal and genetic analysis to the highest levels of accuracy necessary for wide dissemination of PGD. A system of reference centres organized on a regional or even national basis may have to be developed to provide the quick and accurate analysis needed.

A second important technical factor is the state of genetic and genomic knowledge. The most prevalent single-gene disorders have now been identified, and PGD is available for most of them. With most of the low-hanging genetic fruit now having been picked, scientists will have a harder time identifying other single gene mutations for diseases and non-medical traits that are of potential interest to future parents, particularly since developmental and environmental factors may play a more important role than single genes or clusters of genes in causing the chronic diseases of widest concern. Similarly, few of the non-medical traits of apparent interest to prospective parents, e.g. intelligence, height, beauty, memory, longevity, etc, are

likely to correlate with mutations in a few genes or loci that can be easily tested by PGD.

The use of microarrays, which allow transcripts of thousands of genes to be tested at one time, could expand the reach of PGD. However, unless genes predisposing to conditions or traits of interest to prospective parents are expressed at the blastomere stage, microarray tests will be of little use. Even if they can identify single nucleotide polymorphisms (SNPs) associated with those traits, SNP tests of blastomeres might not provide specific enough information for selecting among the relatively few embryos available for testing that are also likely to implant in the uterus. On the other hand, a rapid growth in genomic knowledge and advances in microarray technology could lead to much wider use of PGD for both fertile and infertile couples.

A third factor limiting future use of PGD is its cost. IVF itself is expensive, and adding on PGD will increase that cost. Persons considering reproduction will incur those costs only when the burdens of infertility, the risks of genetic disease, or the desire for a particular trait in a child are great enough to justify the financial and physical burdens of the process. While an argument can be made for national health insurance coverage of basic IVF for infertility (as the UK's NHS has recently done), the case for covering IVF and PGD is a more difficult one (Ashcroft, 2003). It is strongest when a strong health need for PGD exists, for example, to have a matched sibling donor for an existing sick child or to avoid a child with a severe genetic disease, and weakest when sought for non-medical and susceptibility purposes. Because many other projected uses of PGD will not warrant insurance coverage, e.g. PGD for gender variety, those uses will be available only for those with the money to pay for it. Economic factors are thus likely to be a strong limiting factor in the future spread of PGD.

The ethical controversy over PGD

In addition to technical and economic factors, a key factor in determining future use of PGD will be the ethical and social acceptability of creating, screening, and selecting among embryos in order to choose the genetic make-up of offspring. PGD is ethically controversial because of its potential effects on embryos, on persons with disabilities, and on the wellbeing of offspring.

The ethical controversy that surrounds PGD is reflected in differing national policies toward it. Germany and Italy, for example, do not permit PGD for any reason, even though they allow abortion for genetic and maternal indications. The UK, the US, Israel, India, and China, on the other hand, are much more accepting of PGD and are likely to accommodate many extensions of it. Yet even in countries where PGD is permitted, moral controversy about its use, particularly when extended to non-medical indications, will remain.

Embryo status issues

One set of ethical objections arises from those who believe that embryos are already persons or subjects with rights, and should not be created unless they will be transferred to the uterus. Because PGD leads to the discarding of embryos, persons who hold this view strongly oppose PGD. Such

views are largely responsible for German and Italian rejection of PGD for any purpose. However, because many other persons view the embryo as too rudimentary in development to have rights, this objection in itself is not likely to stop greater use of PGD in most countries that do not assign embryos protected legal status.

Selection and eugenics

A second set of objections focuses on the use of PGD to select offspring characteristics, either to avoid children with undesirable genomes or to have children with desirable ones. Some persons object to the unwillingness of prospective parents to submit to the natural lottery. Leon Kass, Chair of the President's Council on Bioethics, and Michael Sandel, a noted political philosopher at Harvard University who is also a member of that Council, have expressed the view that we should not try to change the 'gifted' nature of reproduction by changing or altering the children that we would otherwise have (Kass, 1998, 2000; Sandel, 2004).

If they indeed hold such a view and are consistent in applying it, they should abjure the many ways in which we now select or influence offspring characteristics, such as mate selection, carrier screening, and prenatal diagnosis and termination of pregnancy. It is true that PGD might enable more precise screening at an earlier stage to occur, and could lead to demand for additional non-medical screening. But the notion that we have legitimate interests in the genetic make-up and health of our children is widespread, and will not support across-the-board condemnation of all actions to ensure a healthy birth. If there are objections to the genomic selection that PGD enables, they should be directed to particular uses of concern rather than to condemnation of all uses of PGD.

Another aspect of this set of objections appeals to the animus now widely held against 'eugenics'. Broadly speaking, all PGD is eugenic, in that it selects offspring because of the genes they are expected to carry, but then so is prenatal diagnosis, and to a less specific degree so is carrier screening and even assortative mating. But these forms of eugenic selection do not operate coercively, as did the governmental programmes of the 1920s and 1930s in the US, Germany, and other countries that sterilized 'mental defectives' or other undesirable groups to prevent the spread of 'bad genes' that would sap the public's strength.

Groups representing persons with disabilities have also opposed the dissemination of techniques that enable parents to avoid offspring with genetic disease. They have argued that the very presence of those techniques ends up denigrating or hurting disabled persons, and for that reason alone should be discouraged. They fear that physicians, genetic counsellors, and insurance companies will promote PGD to screen out persons with disabilities in order to 'protect' parents or to minimize insurance costs. They also decry the one-sided presentation of the choice facing parents at risk for such conditions, in which the rewarding experiences of parents who raise children with disabilities are seldom mentioned.

Although the concerns of the disability community do not justify barring the use of PGD, they do underscore the need for policy makers, healthcare providers, and insurance carriers not to promote PGD in ways that denigrate persons with disabilities. In addition, the right of parents not to use PGD for genetic reasons should also be protected.

Offspring welfare

A third set of objections focuses on the effects of choosing offspring genes on those offspring. Sometimes it is said that such choices will 'commodify' children or embryos, for example, conveying the notion that persons will view embryos and prospective children as objects to satisfy parental wishes without needs of their own. It is also rooted in the broader concern that selection of a child's genes will undermine that child's welfare by allowing parents to implement rigid expectations of how the child will grow and develop. The fear is that parents who choose the genome of offspring will impose a set programme for the child's education and development that will prevent the child from determining its own identity (Davis, 2001).

This objection is based more on speculation about worst case scenarios than on empirical data about how parents who use PGD are likely to treat their children. Indeed, there is no reason to think that genetic selection through PGD poses any greater danger to offspring welfare than the other ways in which parents attempt to mould and shape children through education, tutoring, camps, etc. More plausible is the expectation that parents will be equally committed to the wellbeing of their child, regardless of whether they have used PGD to avoid or to have a child with a particular genome.

Ethical acceptability of PGD

In my view, none of the ethical objections is sufficient to bar or condemn all prebirth selection of offspring genetic traits, whether through PGD or other means. As noted, the US, the UK, and many other countries now accept PGD to screen for aneuploidy or Mendelian disorders, and have accepted or are likely to accept extensions that provide medical benefits.

A striking example is the rapid acceptance of PGD for human leukocyte antigen (HLA) matching with existing children, so that the second child may be a source of haematopoietic stem cells for the first child. Initial uses of PGD for this purpose garnered widespread publicity and ethical hand wringing about the dangers of having a child as 'a mere means' to help an existing child. Although available without limitation in the US, the UK's Human Fertilisation and Embryology Authority (HFEA) was willing to license PGD for HLA matching only when the second child was also at risk for inheriting the disease affecting the existing child (HFEA, 2002).

Strong opposition from families of children with sporadic disease and their physicians has led the HFEA to reconsider its position. A review of the authority's original rationale – that donating to a child with sporadic but not inherited disease used the selected child as a mere means – simply did not withstand close ethical scrutiny. As a result, the HFEA now grants licences for HLA matching regardless of whether

the tested embryos are also at risk for inherited disease, as do most other countries where PGD is practised.

A methodology for assessing new uses of PGD

But even though the ethical arguments against all uses of PGD are not convincing, one may legitimately raise questions about whether new uses that stray from a medical model should also be accepted. Much more problematic than using PGD for late-onset and susceptibility screening or for HLA matching for an existing sick child is the use of PGD to screen for non-medical selection of gender and other traits.

How should demand for new uses of PGD, particularly non-medical uses, be handled? A useful approach for physicians, ethicists, and policy makers is to apply a decisional methodology that asks two questions: 'Are parents making the type of decision that falls within common understandings of procreative liberty?' and 'If they are, would those decisions impose harm or burdens on others that justify discouraging or barring them?' A focus on these two questions offers a way to resolve many of the quandaries that new uses of PGD might present (Robertson, 2003).

The first question assumes that persons in liberal societies have a broad range of procreative freedom – the freedom to decide whether to reproduce or not to reproduce. Because reproductive decisions often turn on the expected child-rearing experiences that reproduction will bring, some choice over the genome of prospective offspring should fall within the scope of procreative liberty. If so, prospective parents should be free to obtain and act on information about a prospective child's health and make-up in deciding whether or not to reproduce (Robertson, 2003). While such an approach allows freedom for a wide degree of selection, it still imposes limits. For example, if the selection decision is not reasonably related to fulfilling the traditional parental goals of having healthy offspring to rear, as arguably reproductive cloning when fertile and intentional diminishment of offspring traits do not, then making such decisions may not fall within an individual's procreative freedom.

After a determination that parental procreative freedom is involved, attention shifts to the question of whether the proposed use threatens such significant harm to persons that banning or discouraging that use is justified. The strongest basis for protection from harm would be protecting the welfare of offspring. In many instances, however, protecting the child from harm would prevent its existence altogether. If the child in question cannot be born other than in the condition of concern, some other basis than harm to that individual child must be sought to condemn that action (Robertson, 2004). If that basis cannot be found, then harm to the child or to others may not be a sufficient basis for condemning a new use of PGD.

Close attention to these two questions (the importance of the choice to parents and of harm to others) provides a responsible way to work through most of the ethical issues posed by new uses of PGD and other reproductive and genetic technologies. To illustrate, consider how this methodology would apply to two controversial extensions of PGD: the use of PGD for non-medical sex selection and for choosing to have or avoid having deaf children.

PGD for gender variety

Some couples who have had two or more children of one sex often express a desire to have a child of the other sex. Indeed, they may be willing to reproduce again only if they can be assured that that child's sex will be opposite to that of existing children. The demand is often spurred by wives who have had two or more boys and want the experience of raising a girl as well. Sometimes couples want to have two children – a girl and a boy – and would be willing to use safe and effective selection techniques for that purpose. Psychologists have confirmed what people have long known – that males and females differ in important ways, and that raising a girl is different from raising a boy. The desire for gender variety in one's children seems to be a legitimate desire that rationally falls within common understandings of the choice of parenting experiences that couples may want (Robertson, 2001).

The HFEA, however, conducted a public consultation on non-medical sex selection that was quite dismissive of this desire, treating it as if it were an excessive or improper interest that could affect the wellbeing of the child (HFEA, 2003). In my view, its analysis did not give adequate consideration to the differing rearing experiences that male and female children offer and the legitimate desire of some couples to rear offspring of both sexes. As a result, it allowed the majority opinion against such choices identified in its survey to override the interests of those persons who strongly desire to have a child of the opposite sex to existing children.

Given the legitimacy of the desire that some parents have for gender variety in their children, one may still ask whether satisfying that desire could impose costs on others that would justify limiting its availability. A main concern with any form of non-medical sex selection is its potential for reinforcing the widespread sexism that favours men over women. But male-favouring sexism is a danger only if sex selection leads to men being chosen over women or otherwise disadvantaging women. Whether or not choosing the sex of the first child would entail such effects, it is safe to say that selecting only the sex of a second or subsequent child in order to introduce gender variety into a family ('family balance' in the words of some) has little chance of creating such an effect, will not skew sex ratios, and is apparently acceptable to most feminist writers on the topic (Mahowald, 2000; American Society of Reproductive Medicine, 2001). Arguments that choosing the sex of the child will lead to unrealistic or rigid demands on children of the chosen sex are also unconvincing.

Another source of harm might come from the methods used to create gender variety. Most objectionable would be abortion for sex selection, while least objectionable should be safe and effective prebirth methods, which flow cytometry sperm sorting appears to be. Using PGD to achieve gender variety does require a woman to undergo ovarian stimulation and retrieval, and embryos to be created, screened, and eventually discarded. But these effects alone should not condemn the use of PGD for gender variety. Creation of surplus embryos occurs in routine IVF and in screening embryos for Mendelian disorders, and should also be acceptable for those who undergo IVF and PGD to raise children of both sexes.

PGD and the deaf

The same methodology and analysis may be applied to the use of PGD for genetic mutations related to deafness. Mutations in the connexin genes that affect inner ear hairs appear to account for a large percentage of inherited deafness (Nance and Pandya, 2002). These mutations are inherited in an autosomal recessive Mendelian manner. With the development of sign language contributing to assortative mating among the deaf, mutations in genes predisposing to deafness continue to exist in the population at large. Genetic screening can now identify persons who are carriers of those mutations. Those persons may decide to take their chances and reproduce coitally, use prenatal diagnosis and terminate pregnancies, or even use PGD to identify embryos for transfer that have or do not have those mutations.

If parents request PGD for identifying embryos with these mutations, should it be provided? Persons with inherited deafness in their families or who are otherwise carriers who wish to avoid having an offspring with that condition would be expressing a legitimate parental concern in wishing to have hearing children. Indeed, the absence of hearing is a major disability and would fall within medical uses or conditions. Nor would screening out embryos with deaf-producing mutations stigmatize or otherwise harm existing or future persons who are deaf. Deaf persons are entitled to equal respect under the law. Allowing individuals at risk of having deaf children to use PGD would not diminish that status.

What about deaf persons who wish to have deaf children and request PGD so that only embryos with those mutations are transferred (Levy, 2002; Dennis, 2004)? For those in the deaf community the wish to have a deaf child is a wish to have a child who will continue and share their culture. Nor, strictly speaking, would it harm the deaf child who would not otherwise have been born if his or her parents were not free to make this choice. Although deafness is a disability, it would not prevent that child from having a rich and rewarding life in the deaf culture and community which its parents share. It is difficult to see how its life is so likely to be full of suffering as to make the child's life not worth living. If not, protecting the child would not be a sufficient basis for denying its parents access to PGD for this purpose. However, clinics and physicians would be free not to provide those services if they chose not to.

Conclusion

Demand for PGD is growing because of the significant contribution it makes to the efforts of parents to have healthy offspring. The future growth of PGD and its extension to new uses will depend first of all on the continued development and refinement of blastomere biopsy and analysis, the growth of genetic knowledge, and the development of systems for rapid and accurate assessment of embryonic tissue.

Equally important, however, is an acceptance of the legitimacy, indeed, the right, of parents to create and screen embryos in order to select some of the genetic traits of offspring. Objections based on embryo status, the 'giftedness'

of reproduction, eugenics, and protecting the child's welfare are not convincing grounds to oppose most uses of PGD, if one otherwise accepts that embryos lack inherent moral status and that some parental choice over offspring characteristics is acceptable.

At that point, permitting PGD to be used for new reasons, including non-medical uses, should depend on a careful assessment of the proposed use's importance to the person or couple requesting it and the harmful effects, if any, which it might cause. Analysis of two proposed non-medical uses – for gender variety in a family and for having a deaf child – shows that the case for condemning PGD for those uses is weak. No programme or physician, of course, need provide PGD if they choose not to. But legal and policy authorities, including licensing authorities such as the HFEA, need a stronger case than has yet been articulated for denying willing physicians and parents the freedom to use PGD for those purposes.

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