Britain's new preimplantation tissue typing policy: an ethical defence

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The UK Human Fertilisation and Embryology Authority was right to permit tissue typing preimplantation genetic diagnosis

On July 21 2004, the Human Fertilisation and Embryology Authority (HFEA), Britain's regulatory agency for reproductive technologies, revised its policy on preimplantation genetic diagnosis (PGD) for tissue typing.[1 2] The authority of the HFEA to enact such a policy was affirmed by the UK's highest court, the House of Lords, on April 28 2005.[3] Preimplantation genetic diagnosis combines in vitro fertilisation (IVF) with genetic testing. In PGD, embryos generally undergo biopsy prior to the eight cell stage, followed by genetic testing for a particular trait. Tissue typing PGD is done to identify an embryo that is tissue matched for a child (a future sibling) suffering from a severe disease requiring bone marrow or cord blood stem cell transplantation and for whom no living donor exists. This procedure was first performed in 2000.[4] Precise matching of tissue types is critical to successful tissue transplant, and the donors of such tissues are often referred to as ''saviour siblings''.

Where a tissue matched individual already exists, extracting bone marrow from that individual or collecting cord blood already in storage, rather than creating a match, presents the most immediate treatment alternative. Bone marrow donation from adults or other medically competent individuals is not generally ethically contested, and bone marrow donation from medically incompetent individuals (including children) is also permissible under certain conditions.[5] Where no living tissue donor exists, however, intentionally creating a donor through tissue typing PGD is among a short list of possible treatment options.

The July HFEA policy change makes PGD licensable in cases where tissue typing is the only purpose of testing. Previously, PGD was licensable in the UK only for disease testing, and tissue typing PGD was permissible only when it occurred in conjunction with a disease test.[6] The HFEA's original policy was founded primarily on concerns about the physical safety of children conceived through tissue typing PGD. Cases of tissue typing PGD—both in combination with, and in isolation from, disease testing PGD—have drawn considerable media attention and public interest. Likewise, the HFEA's recent revision in policy has triggered significant criticisms as well as support.

Despite its critics, the HFEA's change in policy represents a triumph for British bioethics regulation and a policy worth emulating in other jurisdictions. This article defends the HFEA's revised policy on tissue typing PGD by reviewing the ethical arguments surrounding this practice. Claims about the ethics of tissue typing PGD are herein divided into two categories: the potential harms of tissue typing PGD to the future child and its family, and the potential harms to society at large should tissue typing PGD become widely practised. The starting point for this analysis is the HFEA's accepted regulatory stance—that PGD may be an ethically acceptable technology (as in the case of disease testing); I will not attempt to argue that disease testing PGD is (or is not) ethically acceptable. Ultimately, this article shows that tissue typing PGD is an ethical procedure, and thus that the HFEA reached the appropriate conclusion in its July 2004 policy revision.

POTENTIAL HARMS OF TISSUE TYPING PGD TO THE FUTURE CHILD AND ITS FAMILY

Safety concerns for the embryo

In arriving at its new policy, concerns about the physical safety of children created through PGD were foremost in the minds of HFEA regulators. The HFEA initially concluded that the safety risks associated with IVF and embryo biopsy (interventions required for tissue typing PGD) would only be acceptable if balanced against the potential benefits of identifying and avoiding the birth of a child with an inherited genetic disorder (as with tissue typing performed in conjunction with disease testing PGD).[6] In reconsidering this policy, the HFEA concluded that the risks of these interventions are acceptable regardless of whether tissue typing PGD is done in conjunction with, or in isolation from, disease testing.[6]

In assessing the physical safety risks of PGD to the future child, it is crucial to recognise that embryo death did not concern the HFEA in this context. The Warnock Report, the precursor to the Human Fertilisation and Embryology (HFE) Act, stated: ''though the human embryo is entitled to some added measure of respect beyond that accorded to other animal subjects, that respect cannot be absolute…''.[7] This sentiment has been reconfirmed in a recent report from the House of Commons Committee on Science and Technology, which concluded: ''While it has been argued that there have been many scientific developments and changes in social attitudes, the Warnock Committee's approach to the status of the embryo remains valuable''.[8] Moreover, disease testing PGD involves the elimination of embryos affected with a specific genetic condition, while the existence of cryopreserved healthy embryos following IVF for infertility may result in abandonment or disposal of such embryos.

The primary concern in evaluating risks for PGD is instead the potential for non-fatal negative effects of IVF or embryo biopsy. Some available evidence has indicated that IVF may magnify the risks for major birth defects.[9] Because tissue typing PGD conducted in isolation from a disease test does not involve the potential benefit that disease testing PGD provides—avoiding the birth of a diseased child—the risks of IVF may not be ethically permissible.

The Medical Research Council in Britain recently published a report reviewing knowledge and research gaps in the development and safety of IVF and related techniques. The report concluded that much more data are required before firm conclusions may be drawn about the relative and long term health and safety risks of IVF and related technologies.[10] A lack of standard lab techniques and culture media among IVF clinics further compounds the difficulties of obtaining clear information about the safety of assisted reproduction.

In the context of PGD, the available data are even less clear because they do not evaluate IVF risks for infertility patients separately from IVF risks for PGD patients many of whom are fertile. Infertility can occur in conjunction with other genetic abnormalities. For instance, imprinting errors—a component of IVF linked risks—have been shown to correlate with certain sperm defects.[11]

Consequently, some portion of the additional birth defects observed in IVF babies may be due to genetic defects in the gametes rather than to the safety of IVF.

Available evidence for the safety of embryo biopsy may be clearer, as it is based on considerable research involving both non-human and human embryos. Findings in animal trials suggest the safety of embryo biopsy,[12 13] as does subsequent research on human embryos.[14] Moreover, in reconsidering its policy on tissue typing PGD, the HFEA undertook a lengthy review of available evidence on the safety of interventions required for PGD (including embryo biopsy).[15] The report concluded that, although more data are required, available evidence suggests the safety of embryo biopsy and of PGD.

Other recent studies of PGD outcomes have concluded that the risk of birth defects is no greater for PGD babies than for those conceived naturally, indicating that neither IVF nor embryo biopsy poses a serious threat to embryos.[16 17] Although these findings may not be exhaustive or entirely conclusive, the latest data suggest the overall safety of PGD. The HFEA now supports these findings, having concluded that there is little scientific ground on which to prevent tissue typing PGD.

Furthermore, even if there were demonstrable safety risks, it is possible that these risks would be insufficient cause to prohibit tissue typing PGD, while still allowing disease testing PGD to continue. Sheldon and Wilkinson have argued in this journal that it is a mistake to consider children born following disease testing PGD as the recipients of any significant benefits different from those accruing to children born following tissue typing PGD.[18] As the HFEA's initial policy for tissue typing PGD indicated, disease testing PGD is generally assumed to deliver significant benefits to the future child by preventing the birth of a diseased child. On this understanding, tissue typing PGD differs from this model in that the primary benefits of the procedure are assumed to fall to the sibling in need of a tissue transplant rather than to the future child.

Sheldon and Wilkinson remind us, however, that PGD does not alter the DNA in an embryo in any way; this means that if a given embryo is found to be disease free following PGD, then that embryo would have been disease free even in the absence of the PGD test. Thus, no direct benefit accrues to a specific embryo through PGD of any kind, other than increasing the embryo's probability of being returned to the womb for development, and this benefit only applies for an embryo of the desired genotype. For a given embryo, the harms and benefits of selection are equal in tissue typing PGD and disease testing PGD. Safety considerations warranting the prohibition of one PGD procedure would speak equally strongly against another. As disease testing PGD is permissible and ethically acceptable in the UK, Sheldon and Wilkinson argue convincingly that concerns about the physical safety of children created through PGD may not be sufficient to prohibit the use of PGD for tissue typing.

Instrumentalisation at conception

Many critics of the HFEA's new policy have focused on the supposed instrumentalisation of the embryo selected through tissue typing PGD for development. As Kevin Male, spokesperson for the British antiabortion group Life, explained: ''In essence a white coated technician brought this human being into the world simply as a means to an end''.[19] For Male and his supporters, the wrongness of tissue typing PGD stems from the fact that it is a procedure undertaken simply for the benefit of another. The embryo is subjected to PGD not to ensure the birth of a healthy child, but in order to serve the need of a sibling for a tissue matched donor.

The charge of instrumentalisation has come from a variety of different perspectives. Most often, however, claims about instrumentalisation rely on Kant's universal prescription to ''act that you use humanity, whether in your own person, or in the person of any other, always at the same time as an end, never simply as a means''.[20] Essentially, in the context of assisted reproduction, Kant's dictum demands that a child be wanted for her own sake, and not simply for sake of others.[21] Conceiving a child in order to harvest her bone marrow or cord blood stem cells is unethical when it treats the child solely as a means to the end of saving her sibling's life.

Marshalling Kant in this fashion is, however, problematic in two ways. First, it is not clear that Kant's categorical imperative applies to embryos or future children. Kant defines personhood with reference to rationality, which is a characteristic neither embryos nor abstract future persons exhibit. Second, even if we allow Kant's dictum to be applied in this case, Male's criticism fails because it is not necessarily the case that parents pursuing tissue typing PGD will conceive a child simply as a means to an end. Male's criticisms reflect a lack of appreciation for the distinction between using someone as a means to an end and using someone *simply* as a meanss to an end. Society might legitimately condemn the parents whose only care for a child conceived through tissue typing PGD is for the stem cells the procedure will generate to save their sick child's life. If this were so, the child would be conceived *simply* as a means to that end. It is not true of necessity, however, that parents seeking tissue typing PGD will have such simplistic motives. Families whose tissue typing PGD applications have come before the HFEA have stated a desire to have additional children, as well as the wish to aid their sick child through selecting a matched donor embryo.[22] Indeed, it is reasonable to believe that parents willing to go to such extraordinary lengths to save their existing sick child are likely to be the sort of parents who would care deeply for each of their children in their own right.[23] Although the use of tissue typing PGD cannot provide absolute certainty that parents will view their future child with the same love and respect as their existing child(ren), neither can it prove the opposite. The use of the tissue typing PGD procedure should not be deemed prima facie evidence that the parents are conceiving their future child simply as a means to an end.

Instrumentalisation after birth: exploitation and coercion

Lord Robert Winston, a prominent doctor and a critic of the HFEA's initial tissue typing PGD policy, stated that in approving tissue typing PGD, ''we would be producing a child that would have been born with completely the wrong expectations for it. It would be beholden to the older sibling and could not be a child in its own right.''[22] Specifically, Winston envisioned a child that, once born, would be forced to serve as blood donor to its sibling all its life.[22] (Interestingly, Winston now supports tissue typing PGD.[24]) Other groups expressed similar fears, predicting a scourge of babies bred for spare parts.[25 26] One group of authors asserted: ''the donor child is at lifelong risk of exploitation, of being told that he or she exists as an insurance policy and tissue source for the sibling, of being repeatedly subjected to testing and harvesting procedures, of being used this way no matter how severe the psychological and physical burden, and of being pressured, manipulated, or even forced over protest.''[27]

Because tissue matched siblings serve as the best possible donors for any kind of tissue or organ transplant, fears about the future coercion or exploitation of one child for the benefit of another are not without merit. Such claims about the fate of the future child ignore the aim of tissue typing PGD, however, as

well as the status of tissue donation by minors in law and ethics. Tissue typing PGD seeks to use the stem cells available in the umbilical cord of the newly born child. The harvest of the necessary tissue is not harmful to the newborn child (or its mother). Ordinarily, the umbilical cord is considered waste material and would otherwise be discarded.

Nevertheless, in the event that the cord blood transfusion failed, the infant might become a candidate for bone marrow donation. From the beginning, the HFEA recognised that although it ''could not place conditions on a treatment license that would allow them to stop any future bone marrow transplant from taking place…there were procedures designed to protect child bone marrow donors in place already and such a child would enjoy the same protection as any other child…''.[28] A child born through tissue typing PGD is no different from any other child in the eyes of the law, and the same rights, responsibilities, and protections apply. Although present UK legislation does not speak explicitly to tissue and organ donation by minors, it is extremely unlikely that a court would approve the harvesting of non-replaceable organs from a minor[29]—a restriction on organ procurement common in other European and international policies. Thus, just as no naturally conceived tissue matched child could legally function as a source of spare parts for its sibling, no child intentionally conceived as a tissue match could legally fill such a role.

Psychosocial harms after birth

In addition to fears of actual physical coercion of the future child, critics of tissue typing PGD have also expressed concerns that the future child will experience emotional and psychological harms as a result of being born, even in part, for someone else's benefit. Both the HFE Act,[30] and the HFEA *Code of Practice*,[31] reflect this concern about the psychosocial wellbeing of children conceived through assisted reproductive technologies by requiring that practitioners and regulators make an evaluation of the ''welfare of the child'' before proceeding with treatment. The sources of potential psychological harms are many and include fears that the future child may feel that she is nothing more than a source of spare parts for her sibling,[27] may experience feelings of inadequacy if the stem cell transfusion is unsuccessful,[32] or may lose some sense of unconditional love from her parents by being born in part to serve an identifiable purpose.[33]

These remain at best speculative fears because no one knows quite what the psychological effects of having been conceived through tissue typing PGD might be. Tissue typing PGD has only been possible since 2000, meaning that the oldest children born through this procedure have yet to reach adolescence, when children undergo separation individuation—learning to be psychologically independent from family and seeking one's own identity[34]—which may be more difficult for children conceived, in part, as tissue donors for family members. Psychosocial data from teenaged children conceived through tissue typing PGD are critical to assessing the real harms and benefits of being born in part to serve as a tissue donor. Thus, we should not downplay or ignore fears about the potential psychosocial harms of tissue typing PGD, however speculative; indeed, we should be monitoring their occurrence. This emphasis on further study and monitoring is consistent with the conclusions reached by the HFEA in its 2004 report on tissue typing PGD.[15] Lack of conclusive evidence notwithstanding, we should not allow speculative concerns to dictate present policy.

Moreover, the Ayala family is an interesting test case for psychological speculations about ''saviour siblings''. In 1990, the Ayalas were the first family to ''go public'' with their attempt to have a child that could serve as a tissue donor for their sick older child, Anissa.[35] Today, Marissa Eve Ayala, Anissa's ''saviour sibling'', is a happy, healthy, normal, and loved teenager and a positive example of the psychological impact of being a ''saviour sibling''.[36] Although Marissa Eve was conceived without the aid of tissue typing PGD, the psychological ramifications of her conception are likely to be similar to those of tissue typing PGD children. Although the Ayalas' experience does not prove that positive psychological effects will always result with the purposeful creation of a donor sibling, it does demonstrate that negative consequences need not follow.

The ethics of the alternatives

Where no living tissue matched donor exists, one possible way forward is to create a donor through natural conception, where there is a one in four chance that the resulting child will be tissue compatible to her sibling and, therefore, able to serve as a possible tissue donor. Parents unwilling or unable to employ tissue typing PGD might choose to take the genetic gamble offered in natural conception (in many cases, parents seeking permission in the UK to pursue tissue typing PGD have already taken – and lost – this gamble).

One British family, the Whitakers, took this gamble and had a daughter that is not tissue matched to their ill child. Another British family, the Hashmis, gambled twice, once giving birth to an unmatched child and once aborting a fetus that would have suffered from the same heritable genetic disorder as its older brother for whom a tissue donor was sought.

In many ways, naturally conceiving a tissue matched donor might seem to be less ethically controversial than purposefully selecting a match. Natural conception requires no medical intervention, and therefore it falls more directly within the reproductive rights of the parents. Whether the motives of the parents are ethically questionable in this case is generally outside state interests, as parents are free to reproduce for whatever reason or for no reason at all. Conceiving a child in order to save the life of its older sibling is a much more worthy goal for reproduction than some others about which the law is silent—for instance, having a child to ''save'' a failing relationship or to carry on the family name.

Natural conception to produce a tissue matched sibling may, however, be paired with prenatal diagnosis to determine the fetus's tissue type prior to birth. In these cases, parents have sometimes, though rarely, been prepared to seek abortion of a fetus that does not bear the desired tissue type.[37] In Britain, natural conception followed by prenatal diagnosis for tissue type and termination of pregnancy is a legally available option for parents.[38] This process imposes considerable physical and psychological risks for conceiving couples, particularly women who must carry (and possibly terminate) the fetus.[39] Moreover, in a culture that accords developing human life respect and consideration in proportion to its development of human characteristics,[7 8] abortion—the elimination of a fetus—must necessarily be less ethically acceptable than PGD, which may result in the elimination of embryos. In its evaluation of tissue typing PGD, the HFEA ethics committee acknowledged: ''In considering alternatives to the proposed class of treatments…the approach of natural conception combined with selective abortion until a suitable pregnancy was identified through (postimplantation) prenatal diagnosis is much less acceptable''.[40] Thus, although natural conception may be preferable to planned embryo selection, the selective forces employed to ensure the presence of the desired tissue type are much less acceptable in cases of prenatal diagnosis as compared with preimplantation diagnosis.

POTENTIAL HARMS OF TISSUE TYPING PGD TO SOCIETY AT LARGE

Enhancement and the slippery slope

One of the HFEA's primary responsibilities is to balance the interests of private individuals in making reproductive choices against the interests of society at large in imposing restrictions on those choices. Traditional PGD aims to ensure the birth of a child that is free from a specific genetic disorder. With tissue typing PGD, selection is for a trait with no known health benefits for the embryo that is biopsied and implanted; instead the goal is to generate cord blood stem cells (and potentially other tissues, such as bone marrow) needed to treat an existing and sick child. For some, this shift opens the door for the use of PGD to select for non-medical traits, including intelligence, appearance, and behaviour.[23 41]

To be sure, tissue typing PGD is a new brand of PGD, in so far as the benefits and burdens of IVF and embryo biopsy fall on different individuals. Tissue typing PGD does not promote the birth of a healthy child, where, in the absence of PGD, a child suffering from a hereditary genetic disorder might have resulted. This difference in intention does not, however, irrevocably lead to non-medical applications of PGD technology. There is no connection between choosing a trait that benefits another (as in tissue typing PGD) and choosing a non-medical trait that benefits the self (as in enhancement PGD). In equating tissue typing PGD with enhancement, these critics misdescribe the shift in policy enacted by the HFEA. The HFEA's 2004 policy does not permit a shift in focus from health outcomes to enhancement; instead, it permits a shift in focus from the health of the biopsied embryo to the health of another—admittedly a controversial shift, but not of the kind identified by people concerned about enhancement and the slippery slope. Disease testing PGD is designed to secure healthy children. Tissue typing PGD is aimed at that same end.

Discrimination

At least one author has linked tissue typing PGD to increased discrimination against the disabled. ''[A]ttitudes may be fostered that promote discrimination against the sick or disabled because they were not 'designed' properly prior to birth''.[42] Interestingly, this claim is more often levelled at disease testing PGD because that procedure intentionally selects against individuals bearing disease causing traits. By contrast, tissue typing PGD aids in treating an illness already present in another individual. It seeks to improve the condition of the individual suffering from disease, not eliminate her. Tissue typing PGD makes cord blood available for transplant, which is an ethically acceptable treatment for these conditions. The treatment goal inherent in tissue typing PGD indicates that it may be *less* discriminatory toward disabled persons—and therefore less slippery—than its disease testing counterpart: ''the explicit purpose of the treatment is to cure a (particular) condition that already exists, not to eradicate the condition from the gene pool''.[42]

Perhaps significantly, the selection for tissue type itself does not affect the future child in any meaningful way. The child will not be taller, shorter, thinner, fatter, or anything else as a result of PGD. She will simply be able to provide the cord blood stem cells necessary to save her sibling's life. The aspect of non-personal benefit inherent in tissue typing PGD insulates the procedure from many of the slippery slope risks inherent in other proposed forms of genetic selection.

Allocation of scarce resources

Britain provides full health benefits for its citizens, sometimes including IVF and PGD. At present, women between the ages of 23 and 39 are eligible to receive one cycle of IVF covered by the National Health Service.[43] The HFEA's decision to license tissue typing PGD may create pressure to expand PGD coverage under the National Health Service. Although a discussion about the economics of tissue typing PGD has not yet been advanced, there should be some evaluation of the relative costs of funding this procedure in a publicly funded health system. When there are hundreds of thousands of patients with various health needs, allocating resources to tissue typing PGD requires evidence that it is a reasonable expenditure of finite public healthcare resources.

Tissue typing PGD is, in fact, cost effective. The lifetime treatment costs for a single patient suffering from beta thalassaemia (one disease treatable through cord blood transfusion) is estimated at more than £200,000.[44] The treatment costs for many other conditions that tissue typing PGD can help treat are likewise prohibitive. Conversely, an IVF cycle with PGD can cost £4,000 to £7,000,[45] or roughly £3,000 more than the costs of traditional IVF.[46] Given the moderate successful pregnancy rates for PGD (23–35%, in part depending on the medical indication for which PGD is used[17]) it is likely that patients pursuing tissue typing PGD will need to undergo multiple treatment cycles to achieve a successful pregnancy, yielding higher costs ranging from £12,000 to £28,000. The extraction and transfusion of bone marrow costs approximately £35,000 to £80,000,[47] with the equivalent processes in cord blood stem cell transfusion being substantially less expensive.[48] In other words, the cost of tissue typing PGD, including the postnatal treatment costs associated with cord blood collection and transfusion, will likely be less than half the lifetime treatment costs of caring for a sick individual, even if pregnancy results only once in three IVF cycles. Thus, tissue typing PGD represents a cost effective treatment option when no matched donor exists.

CONCLUSION

Given the available data, the HFEA's new policy on tissue typing PGD is undeniably more fair and ethical than its previous, bifurcated policy distinguishing between tissue typing PGD performed in conjunction with, versus in isolation from, disease testing PGD. The House of Lords has also recently issued a ruling affirming the HFEA's jurisdiction in regulating and licensing PGD. Although more data are needed about the physical safety and psychosocial risks of tissue typing PGD, a lack of conclusive evidence at present should not trigger the prohibition of a demonstrated lifesaving procedure. Current data suggest that PGD is likely to pose minimal physical health risks for proper fetal and postnatal development, whereas anecdotal evidence about the psychological impact of being born as a donor sibling includes favourable early reports. These concerns deserve continued study and reconsideration, but patients seeking tissue typing PGD should be permitted to proceed with appropriate oversight. This is precisely the conclusion that the HFEA reached in reassessing its policy for tissue typing PGD.

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