

HFEA Consultation: Medical Frontiers

HFEA

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These are the recorded submissions for Session 1. Only sections to which responses have been recorded are listed below.

Permissibility of new techniques

Q1: Having read the information on this website about the two mitochondria replacement techniques – maternal spindle transfer and pro-nuclear transfer, what are your views on offering (one or both of) these techniques to people at risk of passing on mitochondrial disease to their child? You may wish to address the two techniques separately.

Your response:

These techniques would provide further alternatives for women with known 'mitochondrial disease' to have a 'genetically related' child but to avoid transmission to their offspring (see Jones and Holme 'Relatively (im)material: mtDNA and genetic relatedness in law and policy', Genomics, Society and Policy journal, forthcoming 2013). Of the two techniques, some may prefer maternal spindle transfer over pro-nuclear transfer as the former does not involve the creation of embryos which will later be discarded. However, pro-nuclear transfer is not unique in this regard. Hence, opposition to this technique based solely on this consideration may not garner much weight – especially given the rates of use of IVF as compared to the likely uptake of mitochondrial replacement techniques in the future. Clearly there should be concerns about the safety and efficacy of both techniques, which should not be used in treatment cycles until shown to be 'acceptably safe' (highlighted by the NCOB in its 2012 Report). As with the development of IVF, PGD and associated techniques, there is no possibility of carrying out an entirely risk-free pilot study, albeit numbers of treatment cycles can be kept deliberately small at the outset. Therefore, one driver for choosing whether or not one or both techniques should be permitted ought to be the levels of estimated risk (for both techniques) following completion of appropriate research currently being undertaken in this field. We are unconvinced about the use of the slippery slope argument (ie that permission to use mitochondrial replacement will necessarily result in the permissibility of nuclear DNA modification in the future). However, if mitochondrial replacement is made lawful, then the legislative/regulatory drafting will need to be sufficiently robust to ensure that it only permits mitochondrial replacement and not nuclear DNA modification. S.3ZA(5) HFEA 1990 states that regulations may provide for an egg/embryo to be 'permitted' for use in treatment: 'even though [it] has had applied to it in prescribed circumstances a prescribed process designed to prevent the transmission of serious mitochondrial disease.' Mitochondrial disorders can be caused by problems in a person's nuclear DNA, so the 'prescribed process' should be clearly defined to exclude nDNA modification. If this is achieved then further legislative change would be required to permit the 'slip' from mitochondrial replacement to nDNA modification.

Changing the germ line

Q2: Do you think there are social and ethical implications to changing the germ line in the way the techniques do? If so, what are they?

Your response:

We are aware that there is some debate as to whether mitochondrial replacement techniques ought to be typified as germline modification. Arguably mitochondrial replacement is a well defined specific case, set within defined governance regarding research and therapeutic use. However, it is caught by accident in international conventions due to their focus on cloning and concerns regarding 'human dignity'. Therefore, decisions about mitochondrial donation might prove useful, relevant and influential over broader germline modification questions in the future, e.g. via incrementalism; but, germline modification is a fairly indefinite wider landscape. Therefore while it is possible to undertake a risk/benefit calculus on mitochondrial donation alone (with the benefit of appropriate research) – there is certainly an argument that if key moral questions in this context are not addressed, then we may face other problems in the germline modification arena in the future. We believe that the inter-generational modification of the matrilineal germline is worthy of further consideration. Unlike most other types of donation, ie organ, tissue, blood and other bodily materials, mitochondrial donation not only alters the recipients' genetic germ line, but – for female offspring who go on to have their own children – this change is inter-generational. At the very least consideration of the risk of actual harm to both the child and future generations merits close scrutiny. However, not all inter-generational impacts should be treated with suspicion. Promoting good preconceptional nutrition, including interventions such as folic acid supplements to reduce the risk of neural tube defects, is clearly designed to have an inter-generational impact. The issue

cannot be one of consent from the future generations as this could never be obtained, irrespective of the technology. Rather it relates to issues of increased uncertainty over longer term impacts, particularly when linked to irreversibility. In relation to the avoidance of the very serious diseases for which mitochondrial donation is currently envisaged it seems reasonable to regard the benefits as worth obtaining if the technology can be demonstrated to be effective and safe for the first generation child. However, monitoring of any adverse effects on subsequent generations would seem important and this implies a registration system so that follow up is possible.

Implications for identity

Q3: Considering the possible impact of mitochondria replacement on a person's sense of identity, do you think there are social and ethical implications? If so, what are they?

Your response:

We could not agree on a single response to this question. Some were of the view that they do not, on the current state of knowledge, see that the mitochondrial inheritance is constitutive of personal identity in the way that nDNA is perceived to be. They therefore believe that the avoidance of mitochondrial disease through these techniques should not be seen as altering the recipient's 'identity'. They nevertheless maintain that if the techniques are used, it would be advisable for research to be carried out into the views of recipients so that this assumption can be monitored. An alternative view was that there is clear potential for a person's sense of identity to be 'impacted' by the fact that their conception involved ARTs, and that research is necessary to explore how, if at all, mitochondrial replacement compares/differs to current techniques. It is difficult to state with precision what issues would arise for a given person – not least as questions about identity are largely set by expectations rather than any single, objective or universally recognised 'truth'. Useful comparisons might have been made with the accounts of those who used/were born following cytoplasmic transfer. However, there are no reported follow-up studies of these families (it was not licensed in the UK, and has since been prohibited in some jurisdictions). There are issues between the balance of social vs scientific constructions of identity, with much of the latter focused on the very small genetic contribution provided by mtDNA, and thereby deemed irrelevant to 'identity'. The social constructions of mtDNA re identity are unknown, albeit there may be potentially interesting comparisons to be made with host surrogacy, in addition to the usual comparison made with donor conception. Other ARTs involve 3(or sometimes more) persons, albeit - with the exclusion of cytoplasmic transfer – they do not involve genetic contributions from 3 persons. Therefore, it is not clear that mitochondrial donation will prove so disruptive that it will cause the current paradigms of understanding (re 'social' identity) to fall apart. There may be one exception. For communities where matrilineal inheritance is considered to be especially important, eg for Jewish identity, it is feasible that mitochondrial donation might pose particular difficulties. If so, members of these communities would be able to avoid using these technologies, so it should not constitute a reason to prohibit its use by others.

The status of the mitochondria donor

Q4 (a) In your view how does the donation of mitochondria compare to existing types of donation? Please specify what you think this means for the status of a mitochondria donor.

Your response:

Her status is interwoven with considerations around identity & will potentially have an impact on her and any offspring conceived with her mtDNA. It is important to keep this in mind when deliberating the appropriate legal/regulatory response. The separation of genetic motherhood into major and minor contributors is unlikely to create difficulties for the legal construction of mothers. We believe the current gestational privilege as the solution to maternal status should be maintained & unless the status of 'traditional' egg donors changes in the future would not suggest altering that approach for mtDNA donation. We agree with the NCOB's stance that these women should be treated as egg donors re use of ovarian stimulation drugs & compensation. HEAL members who do not see mtDNA as constitutive of identity agree with the NCOB's conclusion that mt donors should not be given entirely the same status as other egg donors under the current regulatory scheme (ie should not be on the register of information/be identifiable - subject to the establishment of a central register of the procedures undertaken for follow-up purposes). Some HEAL members would prefer to see these women treated as other egg donors, with one exception: the 10 family limit should not be imposed; as unlike with nDNA the relative 'genetic risks' are minimal if multiple families use the same mt donor. Such an approach would recognise the woman's role as an egg donor (further research is required on their views), rather than simply determining her status according to whether she contributed nDNA or mtDNA, which is reductionist. A further benefit of treating mt donors in this way is that they could be recorded on the register of information currently held by the HFEA, thereby avoiding the need to set up a separate system. The NCOB indicated that a voluntary contact register might be set up (akin to UK DonorLink), with

the key benefit being the 'maximum flexibility' for donors and offspring to decide if they wish to be identifiable or not. Given the Govt's reluctance to continue funding UK DonorLink this suggests difficulties may lie ahead in establishing a scheme without public funding. As an experimental technique follow up is needed. Further, people should have a right to know that they were conceived through mitochondrial replacement; and if this information is maintained on a register it is not defensible that other people know but they do not. Enforcement of such disclosure may be problematic.

Q4 (b): Thinking about your response to 4 (a), what information about the mitochondria donor do you think a child should have? (Choose one response only)

Your response:

Option4

Please explain your choice

Your response:

It is unfortunate that only a single response could be chosen. We would have liked to have chosen options 2 and 3 to represent the views of HEAL members.

If we do not think that mitochondrial DNA is constitutive of identity then recipients and offspring do not need access to identifying information about the donor. Accordingly the second option would be appropriate (on the assumption that offspring should know they were conceived in this way).

However, a question remains as to how certain we can be of this stance regarding identity.

However, if mitochondrial DNA is constructed as significant for a person's identity then option 3 is appropriate as it places the mitochondria donor on the same footing as a 'traditional' egg donor (following the removal of donor anonymity in 2005). Hence, whatever information is recorded on the register of information should be passed on to the child in question.

Regulation of mitochondria replacement

Q5: If the law changed to allow mitochondria replacement to take place in a specialist clinic regulated by the HFEA, how should decisions be made on who can access this treatment? (Choose one response only)

Your response:

Option2

Please explain your choice

Your response:

The regulation should be akin to that around PGD, drawing by analogy from established practice.

Should the law be changed?

Q6: In Question 1, we asked for your views on the mitochondria replacement techniques MST and PNT. Please could you now tell us if you think the law should be changed to allow (one or both of) these techniques to be made available to people who are at risk of passing on mitochondrial disease to their child?

Your response:

Yes, subject to the regulatory approach we have outlined, of:

i) approval of classes of mitochondrial disease, ii) maintenance of a register, iii) clarification on donor status, and iv) recipients' rights.

Further considerations

Q7: Are there any other considerations you think decision makers should take into account when deciding whether or not to permit mitochondria replacement?

Your response:

Assuming either technique is to be permitted for human use it is vital that appropriate follow-up studies should be undertaken (and financial resources made available to support the research) to measure the levels of both short and long-term risks, not only to the offspring, but where relevant, to future generations, following mitochondrial replacement. Without such research there will be insufficient data for prospective patients to assess the levels of potential risk vs their desire for a child that is genetically related to them.