Human Fertilisation and Embryology Authority (HFEA): Medical Frontiers: Debating Mitochondria Replacement

Response by the Muscular Dystrophy Campaign

7 December 2012

Key points:

- These are novel techniques with a controversial ethical nature. Given this, we welcome the opportunity afforded by this consultation for public discussion of these new therapies. It is important that information about these novel procedures is available for the public and patients to access.

- It is our view that the benefits of these potential therapies to patients for whom there are few other clinical options outweigh the potential ethical risks.

- The HFEA expert review of the safety and effectiveness of these techniques found that there was no evidence to suggest they were unsafe and recommended further research into mitochondria and the treatments. This expert conclusion is sufficient to begin the process of developing regulations to enable these techniques to be made available once proven safe and effective.

- We fully support the introduction of regulations to enable these techniques to prevent the transmission of serious mitochondrial disease, providing that further research continues to demonstrate their safety and efficacy.

The Muscular Dystrophy Campaign is the leading UK charity fighting muscle-wasting conditions. We are dedicated to beating muscular dystrophy and related neuromuscular conditions by finding treatments and cures and to improving the lives of everyone affected by them.

Our work has five main focuses:

- We fund world-class research to find effective treatments and cures

- We provide practical information, advice and emotional support for individuals with muscle-wasting conditions, their carers and families

- We campaign to bring about change and raise awareness of muscular dystrophy and related neuromuscular conditions

- We award grants towards the cost of specialist equipment, such as powered wheelchairs

- We provide specialist education and development for health professionals.
Question 1. Permissibility of new techniques

Having read the information available about the two mitochondria replacement techniques – maternal spindle transfer (MST) and pro-nuclear transfer (PNT), 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.

We know that mitochondrial diseases are a group of highly variable conditions that can be severely debilitating and disabling, and, in their most serious forms fatal. Approximately 6000 people in the UK are affected by a mitochondrial disease and 3500 of these have a mitochondrial myopathy.

There are currently no treatments available for mitochondrial diseases and the complex way in which the conditions are passed from mother to child makes it difficult for clinicians to provide genetic counselling, or information on disease prognosis.

There are several options available to families that wish to have a child unaffected by a mitochondrial disease. They can adopt a child, they can opt for egg donation or use pre-implantation genetics diagnosis. In case of an adoption the child would share no genetic material with the legal parents and even if families opt for egg donation the future child would share no genetic material with their birth and legal mother. Both options are generally considered by women that have come to terms with their own infertility. Women who have a mitochondrial myopathy, however, do not have any problems with their fertility and therefore often wish to have their own biological children. Pre-implantation genetics diagnosis is offered at some clinics here in the UK and is used to identify embryos that have a low level of mitochondrial mutations. Although this technique will minimise the risk of having an affected child it will not eradicate it. It can also not be used for women that have high level of mitochondrial mutations.

Both maternal spindle transfer and pro-nuclear transfer have the potential to give women affected by a mitochondrial disease the option to have a healthy child. Whilst the techniques are different, both aim to replace the mutated mitochondria with healthy mitochondria (from a donor egg). Both techniques are currently being tested in the laboratory, and although there is some information on their effectiveness in animals, the safety of the techniques are not fully understood.

Based on the current research it is not clear yet whether one technique might be superior with regards to safety and efficacy and therefore it is too early to favour one technique over the other. Establishing that the techniques are safe and optimising and refining each step of each procedure should therefore remain a key aim before they can be tested in clinical trial.

If the techniques both prove to be safe and effective, they both should be offered to families at risk of passing on a mitochondrial disease to their children. It is essential that families are given the appropriate information so that can make their own choice whether and which of the techniques they wish to use. It would be unethical to withhold a treatment that is life-saving, can prevent years of painful suffering and gives families the option of having healthy biological children.

Question 2. Changing the germ line

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?

First we note that the overwhelming majority of the families that took part in the discussion we facilitated did not have any social and ethical concerns using the techniques.
The techniques are seen as an optimisation of a technique that is currently already offered – egg donation. However, children born following egg donation share no genes with the birth mother. In the case of MST and PST the future child would share the whole of the nuclear DNA that carries the genes that determine our physicality and character with their birth mother. Only 13 of a total of 25,000 genes - less than 0.1% of the total DNA - would be taken from the donor. This means that only the minimum of the DNA – the mitochondrial genome - that carries the genetic defect is exchanged. The mitochondrial genes only carry the information for accurate functioning of the mitochondria.

Concerns have been voiced in the public that development of these techniques opens the door for the development of other techniques that would allow the modification of the nuclear germ line DNA. It should be noted that MST and PNT can only applied to women with a mitochondrial disease and cannot be used to modify the chromosomal (nuclear) DNA nor do they represent a step in the development of such techniques. They should be seen as a completely different entity and social and ethical implications should be part of a separate debate. The Nuffield Council of Bioethics concluded that the nuclear germ line DNA is different from the mitochondrial one and we support this view.

Question 3. Implications for identity

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?

As discussed in Q2, MST and PNT are considered to be an improvement of a technique that is currently offered to women that have a mitochondrial disease – egg donation. In case of egg donation the birth mother does not share any genetic material with the future child. MST and PNT, however, potentially offer to women the opportunity to have children that share 99.9% of their DNA. If society does not have any concerns on a child’s sense of identity using egg donation or even adoption then identity issues would certainly be less significant when using MST and PNT.

When families affected by a mitochondrial disease were asked this question none of them had any concerns that mitochondrial replacement could have an impact on their future child’s sense of identity.

Question 4a. The status of the mitochondria donor

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.

We endorse the answer that the AMRC and the Genetic Alliance have given in their response;

Mitochondria donation is a new form of donation. As such, there are a number of unique aspects that should be taken into account when comparing with other existing types of donation:

- This is a single donation which allows a person at risk of a serious condition to avoid that condition and in this sense is similar to bone marrow donation and organ donation in terms of medical gain to the recipient.

- It is a donation which does not confer a significant amount of genetic material to the resulting child and in this sense is not similar to gamete donation in terms of relation of the donor to the recipient.

- It is a donation that allows a couple that otherwise could not to conceive a healthy child and is similar to gamete donation in terms of altruism from the donor and benefits to the couple.

For the same reasons that we do not believe the impact of mitochondria donation on a person’s sense of identity is high, and that social and ethical implications are few, we do not consider the status of a mitochondria donor to be as high as a gamete donor to a donor-conceived child in terms of relatedness and access to identity. Their status in terms of altruism and impact upon the life of the recipient is certainly high, and comparable to organ donation and gamete donation in this sense.
Question 4b. The status of the mitochondria donor

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

- The child should get no information
- The child should be able to get medical and personal information about the mitochondria donor, but never know their identity
- The child should be able to get medical and personal information about the mitochondria donor and be able to contact them once the child reaches the age of 18
- Other
- I do not think mitochondria replacement should be permitted in treatment at all

Please explain your choice:

It is the view of the families that MST and PNT is different to gamete donation as it involves the donation of a much smaller and more insignificant amount of DNA. Because it can be compared to organ donation it is not considered to be necessary to reveal the identity of the donor not to provide personal information about her. The family, however, should be given access to medical information of the donor that relates to mitochondrial diseases for the lifetime of the donor. As such the parents/child will be made aware if the donor herself was affected by a mitochondrial disease due to a genetic defect in the mitochondrial genome that was either undiagnosed or undiscovered at the time of the donation.

Question 5. Regulation of mitochondria replacement

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)

- Clinics and their patients should decide when mitochondria replacement is appropriate in individual cases
- The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and, just for these diseases, permit clinics and patients to decide when it is appropriate in individual cases
- The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and also decide, just for these diseases, when it is appropriate in individual cases
- I do not think mitochondria replacement should be permitted in treatment at all

Please explain your choice:
The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and, just for these diseases, permit clinics and patients to decide when it is appropriate in individual cases.

The severity of mitochondrial diseases is very variable and the regulator should decide the conditions for which mitochondria replacement is appropriate. This should be done in consultation with clinical experts and patient organisations. Mitochondrial disease, however, can very significantly between individuals even between family members. Whilst clinics will be aware of an individual’s disease progression, severity and symptoms, relying on regulators to assess every individual case is likely to be impractical. Therefore, the decision, the decision whether mitochondrial replacement is appropriate to an individual should be made by the clinic and the patient.

Question 6. Should the law be changed?

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?

The Muscular Dystrophy Campaign has spearheaded the development of this technique by providing more than £1 million towards research lead by Professors Doug Turnbull and Mary Herbert at Newcastle University over the last 10 years. There is currently no alternative treatment available for people affected by a mitochondrial disease and it is imperative to change the current legislation so that the full potential of these techniques can be tested in clinical trial. This will ensure that these potential treatments can be tested in a controlled way within a legal framework and that the clinical trial participants will be protected by appropriate safety standards.

Question 7. Further considerations

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

We wish to emphasise that the often devastating impact of mitochondrial diseases on patients and their families should be borne in mind at all times.