Office for Public Management

Medical frontier: Debating mitochondria replacement

Annex VI: Patient focus group

Report to HFEA

February 2013

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Client	HFEA
Document title	Medical Frontiers: Debating mitochondria replacement: Patient focus group
Date modified	22/02/2013
Status	Final
OPM project code	8984
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Executive summary

The Office for Public Management (OPM), in partnership with Forster and Dialogue by Design, was commissioned by the Human Fertilisation and Embryology Authority (HFEA) to conduct a multi-method research and engagement project looking at the possible social and ethical issues relating to two techniques for the avoidance of mitochondrial disease: pronuclear transfer (PNT)[1] and maternal spindle transfer (MST)[2].

As part of this research and engagement, OPM conducted a focus group in London in December 2012 with six participants, all of whom had been affected by mitochondrial disease in different ways. We also conducted one telephone interview, in January 2013, with a participant who was unable to attend the focus group. Participants reported having spent long periods of time in hospital under the care of doctors, and a great deal of time worrying about having children. Understandably the topic was quite difficult for some participants and they were therefore often overcome with emotion.

The importance of being able to have a healthy child that is genetically their own underpinned participants' attitudes towards **the existing options** available to couples who would like to avoid passing on mitochondrial disease to their children. For example, with regards to preimplantation genetic diagnosis (PGD) and prenatal diagnosis (PND), participants were quick to point out that neither of these techniques guaranteed that children born from using them would be free from mitochondrial disease. With respect to adoption and IVF with donor eggs, many participants felt that whilst these were suitable for some people, they wanted to have children that were genetically related to them.

Participants were overwhelmingly positive about the **new techniques**, particularly because, unlike most of the current options, they could potentially eliminate mitochondrial disease not only for the child, but also from the germ line. They also appreciated that the techniques would enable them to have children that were genetically their own. Those participants that had a less clear understanding of the techniques had some questions and concerns that they were keen to have clarified, for example about the safety and uncertainty of the techniques. In general, all participants emphasised the importance of individual choice in deciding whether to use these new techniques.

Participants were not particularly concerned that the new techniques would result in changing the female **germ line**. They felt that the techniques only changed the germ line in so far as they were 'preventing disease' and that this was essentially a good thing. Participants were also comfortable with parents making this decision on the behalf of children, because again it was about ensuring that the child would be healthy. Participants were very familiar with the potential issue relating to these new techniques employing **DNA from three people**. They rejected the '3 parent family' label - drawing on their knowledge of the science to argue that since no nuclear DNA would be used from a third party, the

[1] Pronuclear transfer involves transferring the pronuclei from an embryo with unhealthy mitochondria and placing them into a donor embryo which contains healthy mitochondria and has had its pronuclei removed. A pronucleus is a small round structure containing nuclear DNA seen within an embryo following fertilisation. A normal embryo should contain two pronuclei, one from the egg (maternal pronucleus) and one from the sperm (paternal pronucleus).

[2] The maternal spindle is a structure within the egg containing the mother's nuclear DNA. Maternal spindle transfer involves transferring the spindle from the intended mother's egg, with unhealthy mitochondria, and placing it into a donor egg with healthy mitochondria.

techniques were more akin to blood or tissue donation and that a child's sense of self would therefore still be inherited from the parents. Participants also felt quite strongly that **donors** should remain anonymous. They also felt that donors would *and* should want to remain anonymous as this would mean that they were doing it for the right reasons. They felt that this was because unlike with sperm or egg donation there was no nuclear DNA that was being donated. Participants identified a number of **key messages** for government about the new techniques:

- The potential for the new techniques to relieve suffering
- The potential for the new techniques to reduce costs to the health system
- The potential for the new techniques, unlike current options, to prevent mitochondrial disease

1. Introduction

Mitochondria are present in almost all human cells. They are often referred to as the cell's 'batteries' as they generate the majority of a cell's energy supply. For any cell to work properly, the mitochondria need to be healthy. Unhealthy mitochondria can cause genetic disorders known as mitochondrial disease.

There are many different conditions that are linked to mitochondrial disease. They can range from mild to severe or life threatening, and can have devastating effects on the families that carry them. Currently there is no known cure and treatment options are limited. For many patients with mitochondrial disease preventing the transmission of the disease to their children is a key concern.

Mitochondrial disease can be caused by faults in the genes within a cell's nucleus that are required for mitochondrial function or by faults within the small amount of DNA that exists within the mitochondria themselves. It is the latter form of mitochondrial disease that could be avoided using two new medical techniques, termed pro-nuclear transfer (PNT)[1] and maternal spindle transfer (MST)[2] which UK researchers are working on.

These techniques are at the cutting edge, both of science and ethics and are currently only permitted in research. They involve removing the nuclear DNA from an egg or embryo with unhealthy mitochondria, and transferring it into an enucleated donor egg or embryo with healthy mitochondria.

The Human Fertilisation and Embryology Act (1990) (as amended) ('the Act') governs research and treatment involving human embryos and related clinical practices in the UK. The Act currently prevents the clinical use of these techniques (or any other technique that involves genetic modification of gametes and embryos to treat patients). However, in 2008 the Act was amended, introducing new powers which enable the Secretary of State for Health to permit techniques which prevent the transmission of serious mitochondrial disease. The Secretary of State for Health and the Secretary of State for Business, Innovation and Skills asked the Human Fertilisation and Embryology Authority (HFEA) to seek public views on these emerging techniques. On considering advice from the HFEA the Government will decide whether to propose regulations legalising one or both of the procedures for treatment.

The HFEA, together with the Sciencewise Expert Resource Centre[3], therefore commissioned OPM (in partnership with Forster and Dialogue by Design) to conduct a multi-method research and engagement project looking at the possible social and ethical issues and arguments relating to the techniques. The project consisted of five strands:

1. Deliberative public workshops
2. Public representative survey
3. Patient focus group
4. Open consultation meetings
5. Open consultation questionnaire

This research provides the evidence base that will inform the HFEA's advice to the secretary of state.

[3] The Sciencewise Expert Resource Centre (Sciencewise-ERC) is the UK's national centre for public dialogue in policy making involving science and technology issues

The **patient focus group** aimed to provide a dedicated safe space where a small number of those affected by mitochondrial disease could make in-depth contributions about their views and experiences. Rather than attempting to highlight the full range of patient and family views and experiences, the focus group and additional interview provides a small scale qualitative 'snapshot' of the varying views of those affected by mitochondria diseases.

This report provides an overview of the key themes and issues that were raised by participants.

2. Overview of participants' backgrounds

OPM conducted one focus group in December 2012 which was attended by six participants, all of whom had been affected by mitochondrial disease in different ways[4]. We also conducted one telephone interview, in January 2013, with a participant who was unable to attend the focus group. Participants were recruited through contacts at patient groups and charities and at the open consultation meetings which were run as part of the project.

A brief background of the participants is provided below.

- **Participants A and B:** A couple who had a daughter with Leigh's syndrome who had passed away last year. They reported that the doctors had informed them that their daughter had acquired the disease not as a result of maternally inherited mitochondrial DNA, but as a result of a combination of the couple's DNA. However, the woman (Participant A) also reported that she had not been tested for mitochondrial disease. The couple are in the process of trying to have a child through IVF with donor eggs, but have been on the waiting list for a year and a half.
- **Participant C**: A mother of five who reported having five children with varying degrees of Mito Partial Complex 1, all of whom were only diagnosed quite recently. She is particularly concerned for her three daughters who are in their late teens/early twenties and whom she worries will not be able to have children without passing on the disease.
- **Participant D:** A woman, who reported having two grandchildren with Mito Complex 1 which had been maternally inherited from her foster daughter. She reported that her foster daughter would not want to have any more children because she does not want to pass on the disease.

[4] Mitochondrial disease can be caused by one of two problems within a cell. Firstly, by faults in the genes within a cell's nucleus that are required for mitochondrial function. This type of mitochondrial disease can be inherited from the father or mother as nuclear DNA is inherited from both parents. Secondly, by faults within the small amount of DNA that exists within the mitochondria themselves. Mitochondrial DNA is only inherited from the mother and helps produce a cell's energy. It is this form of mitochondrial disease that could be avoided using the new techniques.

Mitochondrial diseases vary in terms of severity, depending on the type and extent of DNA defect and the specific gene affected. It also depends on the proportion of healthy versus unhealthy mitochondria within a cell and what type of cell is affected.

Diseases caused by faults in mitochondria may appear at birth or develop later in life. They are usually degenerative and can affect the functioning of muscles and major organs as well as the nervous system and the cardio-vascular system. There are many different conditions that are linked to mitochondrial disease.

- **Participants E and F:** A young woman (Participant E) who reported that she had been diagnosed with MELAS when her maternal aunt had passed away as a result of mitochondrial disease. She felt strongly that she would not want to risk passing the disease on to her children. Her mother (Participant F) also attended the focus group.
- **Interview participant**: A mother who has a son with mitochondrial neuro-gastrointestinal encephalopathy, who was misdiagnosed for many years before the above diagnosis was confirmed at the age of 26. He has had numerous major operations over the years and has been in intensive care and nearly died a few times. A bone marrow transplant from his sister has helped with his recovery, although this recovery is very slow. There is no history of mitochondrial disease in the family. She reported the pain, suffering and disruption experienced by the whole family when a family member is so ill for so long.

Participants reported having spent long periods of time in hospital and under the care of doctors. They also all reported having spent a great deal of time thinking and worrying about having children. Some participants were quite keen to share their experiences and talk about how their lives had been affected by mitochondrial disease from the start of the discussion. Others were initially more reserved but opened up once the discussion progressed and the participants had bonded well as a group. Understandably the topic was quite difficult for the participants and they were therefore often overcome with emotion.

3. Views on the existing options

At the beginning of the focus group participants had the chance to learn about the techniques and the science. This involved reading and discussing a one page briefing paper and watching an animated video[5].

Next, participants were invited to share their views on and experiences of the current options available to couples who would like to avoid passing on mitochondrial disease to their children.

As mentioned above, one couple reported that they were in fact trying to have **IVF with a donor egg**. They had been told by doctors that they had a 25% chance of having another child with mitochondrial disease and felt very strongly that this was not a risk worth taking:

> *"We wouldn't take that risk, it's too high, it's too cruel a disease…to have another child and watch that child die." Participant A*

However they had been unsuccessful so far because of the lack of availability of egg donors. They had been on a waiting list for a year and a half and were both frustrated and disappointed about not having been more successful. They reported having been advised to find their own egg donor, but felt quite strongly that they wanted the donor to be anonymous.

They also reported that given that they are only entitled to one round of IVF on the NHS, they couldn't afford to pay for the treatment privately if the first round failed, as many people tend to do. They therefore felt that this option was better suited to people that were well off and could afford private treatment. Other participants felt that this was not an option they would

[5] As part of the research and engagement project, a short participant briefing video was produced. The video was about 5 minutes long and introduced the science and the new techniques.

consider because, although it may be acceptable and suitable for some people, they were keen to have children that were genetically related to them. The same drawback was also associated with **adoption**, which none of the participants had considered as yet, and about which there was little discussion. The interview participant felt that adoption is really the 'final straw' for families that can't have children by any other means.

With regards to **preimplantation genetic diagnosis** (PGD) and **prenatal diagnosis** (PND), participants were quick to point out that neither of these techniques guaranteed that children born would be free of mitochondrial disease. Some participants also reported that they had been told by doctors or read online that these techniques were only able to identify some types of mitochondrial disease and not others. The interview participant noted that the experience of PND could be very traumatic as it could result in parents having to choose whether or not to terminate a pregnancy if a fetus is diagnosed with mitochondrial disease. No participants had considered using these techniques as yet. Participants reported being *"too terrified"* to try these two techniques. They felt that there was *"too high a risk"* that their children would still also have mitochondrial disease and therefore suffer greatly, as would the rest of the family.

> *"As somebody who has had symptoms and has seen it at its worst…I couldn't do that." Participant E*

> *"The trauma, the upset, the total disruption to normal family life when you have someone in family that is seriously ill." Interview participant*

Furthermore, the two participants (C and D) reported that these two options would not be available to their daughters because embryo screening is not currently permitted in Ireland.

The importance of being able to have a healthy child that is genetically their own therefore underpinned participants' attitudes towards the existing options. The young woman with MELAS (Participant E) felt quite strongly that *"these are not treatments, these are not cures…none of them."* The interview participant agreed with her that these techniques do not represent 'reproductive choice', particularly in light of the fact that there are techniques being developed that can potentially eliminate the disease and allow people to have children that are genetically their own.

> *"They can be right for certain people but it's a matter of choice and if the techniques exist…if there is a way that women can have their own children, if there is a way that can eliminate the disease…then it should be available." Participant E*

> *"If you can guarantee it with another procedure then you would go for that option. Parents want to give child the best opportunities in life, to give them a normal life." Interview participant*

Some participants also reported that most patients are not *"at this stage yet"*, and are still struggling to get confirmed diagnoses and come to terms with the implications. Others drew on their own long and often drawn out experiences of uncertainty to report that all the current options are available only to those who know they have mitochondrial disease. They expressed great concern about people who are likely to have the disease and do not know it.

4. Understanding of and views on new techniques

There were varied levels of understanding about the new techniques amongst the participants, with some having a very detailed understanding of the science involved, and others having a basic understanding as well as lots of questions for clarification. The majority had heard about the techniques online as part of their own research about one year ago. One participant reported that her consultant had in fact told her that the new techniques were in development about three years ago. The interview participant reported that she had heard about the techniques at an event that was part of the HFEA's public dialogue events.

Participants were **overwhelmingly positive** about the new techniques, particularly because, unlike most of the current options, they could eliminate mitochondrial disease not only for the child, but also from the germ line.

> *"Anything that could eliminate even part of mitochondria disease is a wonderful thing…" Participant C*

> *"If either can eliminate the disease so be it…there is nothing more sad than seeing a child that can't join in with rest of society." Interview participant*

They also appreciated that the techniques would enable them to have children that were genetically their own.

> *"It will still be the genes of the mother and father, the child will still look and sound and act like its parents, that's really important." Interview participant*

One participant (Participant E) recognised that the techniques didn't really represent a cure and felt positive that perhaps there would be a cure in the future. However, these new techniques represented the best option available to women now. She remarked that these new techniques *"would change my life."*

> *"We're talking about mothers now and what can be done for them…for right now, this is phenomenal." Participant E*

Participants also felt that the new techniques would save the health system a great deal of money, given how expensive it currently is to care for patients with mitochondrial disease.

Those participants who had a less clear understanding of the techniques had **some questions and concerns** that they were keen to address. For example, one participant (Participant C) had questions about the **safety and uncertainty** of the techniques. More specifically, she had questions about what needed to happen to refine the techniques and how confident scientists were that the techniques would work. She had concerns that the first babies born from these techniques would be akin to an 'experiment':

> *"Imagine being the parents of that first child born this way…it doesn't sit right with me." Participant C*

Other participants disagreed and reported that they would be happy to be the first and that *"it is a risk I'm willing to take…for me the risk is lower than the risk of the disease." Participant E*

Some participants argued that there is always a degree of uncertainty with respect to medical innovation and that this is *"a part of all medical progress"* (Participant D). This led the participants to discuss and agree on the importance of **individual choice** in deciding whether to use these new techniques.

Two participants (C and D) reported that when they had presented these new techniques to a group of approximately 170 parents with mitochondrial disease in Ireland, the response had been mixed with half supporting the techniques and the other half having concerns. The participants felt that the latter group held religious and cultural values and for this reason had some discomfort with the involvement of a third person or donor in the construction of embryos. However, the participants reported that the group that initially had concerns was now *'starting to come around'* after they began to understand the techniques better. One participant (Participant C) reported that her daughter (who has mitochondrial disease) had a *"fear that a little bit of her would be missing."* She reported that she herself, being *"an Irish Catholic girl"* had *"a little bit of reservation"* with the concept of third party involvement, but that if her daughter decided to use these techniques she would fully support her. Again, the importance of **individual reproductive choice** was discussed.

> *"If this isn't right for you…because of your personal beliefs, because of your culture, because of your background, then you don't have to have it…it's about choice."* *Participant E*

One participant also wanted to clarify whether the new techniques could only eliminate those types of mitochondrial disease that were a result of mitochondrial DNA mutations and not those that were the result of nuclear mutations. Although the former was claimed to include the vast majority of mitochondrial diseases, it was also recognised that for the latter group of patients, the new techniques were therefore not helpful or applicable.

5. Potential social and ethical issues

Participants were asked to consider a number of potential social and ethical issues and to comment on the extent to which these issues had an impact on their views on whether these new techniques should be used in treatment.

5.1 Affecting future generations

Participants were not particularly concerned that the new techniques would result in changing the female germ line. They drew on their knowledge of the science of the techniques and argued that the techniques only changed mitochondrial DNA and not nuclear DNA, and that it was the latter that determined inheritable characteristics. They therefore felt that the techniques only changed the germ line in so far as they were 'preventing disease' and that this was, in essence a good thing.

> *"It's not changing the child…It's just making sure it's a healthy child." Participant D*

> *"I have no problem with removing whatever has to be removed and changing the germ line…I don't care." Participant C*

Participants were also very comfortable with parents making this decision on the behalf of children, because again it was simply about ensuring that the child would be healthy. They felt that it was part of their instincts as 'parents' to want to provide their children with the best opportunities in life. One (Participant E) remarked that she would be *"happy for my mum to make this decision on my behalf"* and another remarked that *"I have it and would want my germ line changed"* (Participant F). Moreover, the interview participant felt that future generations may in fact resent their parents for not having used a technique that could have saved them much pain and suffering.

5.2 DNA from three people

Participants were very familiar with the potential issue relating to these new techniques employing DNA from three people. They reported that the media had picked up on this and had reported it in a sensationalist manner. They also felt that the way in which the issue is generally talked about is 'misleading', 'emotive' and 'confusing'. They again drew on their knowledge of the science to argue that since no nuclear DNA would be used from a third party, the techniques were more akin to blood or tissue donation. They stressed that mitochondrial DNA is only involved in energy production and that a child's sense of self would be derived from his/her nuclear DNA which would still be inherited from the parents.

> *"Everything that makes you 'you' and that makes your child 'your child' is not touched…" Participant F*

They also felt that the benefits associated with these techniques were also more important than the downside of not being able to trace maternal ancestry.

> *"How often do you actually want to trace maternal ancestry…? And is that more important than having a healthy child?" Participant E*

5.3 Status of the mitochondrial donor

Discussion about the 'DNA from three people' issue led participants to discuss the status of the donor and whether or not the donor should be able to access information about the child and vice versa. Participants felt quite strongly that donors should remain anonymous. They also felt that donors would *and* should want to remain anonymous as their only motivation should be to help other couples have a healthy child of their own. They felt that this was because, unlike with sperm or egg donation, there was no nuclear DNA that was being donated.

> *"I've donated blood and haven't given a thought about where that's going. There has never been in the press that someone wants to know where the blood came from that saved their life." Interview participant*

Participants C and D were quite concerned because they had read online that donors would in fact be able to access information about the child and were relieved to hear that this was not necessarily the case and that the policy on information access had not been decided.

Participants felt that donors should be well informed and should have to sign documentation agreeing to be anonymous.

6. Key messages

Participants were asked to take a few minutes to themselves to note down the key messages they would like to give the Government regarding the new techniques. A few common themes emerged[6]:

- **The potential for the new techniques to relieve suffering:**

  "Future children would be spared the awful pain, suffering, constant endless hospital stays and spared having bits of muscle cut from their bodies for testing."

  "Parents would not have to watch their children dying slowly, painfully and know that they will not be able to have any more children."

- **The potential for the new techniques to reduce costs to the health system:**

  "If mitochondrial disease was eradicated then it would be one less bill the government would have to pay."

- **The potential for the new techniques, unlike current options, to prevent mitochondrial disease:**

  "The current options are not cures – PNT and MST will for the first time mean that a cure can be offered."

  "Existing options are not treatment or cures. As a matter of preventing transmission of disease and reproductive choice new treatments are ethically acceptable – indeed it would be less ethical and of more risk to prevent further research."

Other messages included:

- The importance of these techniques being tested/trialled in a regulated environment
- The anonymity of the donor
- The importance of mitochondrial disease testing/diagnosis

[6] The key messages for Government were noted down on to post-it notes and so cannot be attributed to the different participants.