The Academy of Medical Sciences' response to the Department of Health's consultation on draft regulations to permit mitochondrial donation

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Summary

In April 2011, the Academy and partner organisations wrote to the Secretary of State for Health calling for the introduction of regulations to enable new techniques that aim to prevent the hereditary transmission of mitochondrial disease caused by mutations in mitochondrial DNA (mtDNA) to be used in clinical practice, if sufficient pre-clinical evidence is obtained.[1] We subsequently welcomed scientific progress made in this field and expressed our full support for the introduction of regulations to permit the use of treatment techniques to prevent the transmission of mitochondrial disease from mothers to children in clinical trials, as outlined in our response to the Human Fertilisation & Embryology Authority's (HFEA) public consultation on mitochondrial donation in December 2012.[2]

The Academy warmly welcomes the Department of Health's consultation on its draft regulations to permit mitochondrial donation, and the opportunity to provide input on these at this early stage. We are encouraged to see a strong set of regulations that address many of the concerns and uncertainties about regulating the use of these treatments that we have previously expressed. In particular, we are pleased to see that Government intends for the HFEA to oversee the licensing of clinics permitted to use the treatments, as well as regulate the administration of treatments to patients on a case-by-case basis.

We are also supportive of the Government highlighting the requirement for long-term follow-up research on offspring born following mitochondrial donation, to monitor the safety and efficacy of the techniques. As such, if the regulations are enacted, we would recommend that the HFEA prepares standards for clinics to follow to encourage the enrolment of patients in follow-up studies and for evaluating and reporting data on studies in which their patients are enrolled. It should make the description of sufficient plans on these aspects by clinics a condition of licensing the use of the treatments.

Introduction

The Academy of Medical Sciences promotes advances in medical science and campaigns to ensure that these are translated into healthcare benefits for society. Our elected Fellowship includes the UK's foremost experts drawn from a broad and diverse range of research areas. A number of our Fellows have expertise in areas related to the study of mitochondria, mitochondrial disease and the development of potential treatments for these diseases. The Academy has been fully supportive of previous developments to bring potentially life-saving treatments for serious mitochondrial diseases into the clinic, including our statement of support for the opening of a new Centre for

[1] The Academy of Medical Sciences (2011). *Treatments to avoid transmission of mitochondrial disease.* http://www.acmedsci.ac.uk/download.php?f=file&i=13427

[2] The Academy of Medical Sciences (2012). *The Academy of Medical Sciences' response to the Human Fertilisation & Embryology Authority's public consultation on mitochondria replacement.* http://www.acmedsci.ac.uk/download.php?f=file&i=13428

Mitochondrial Research at Newcastle, and a response to the Human Fertilisation & Embryology Authority's public consultation on novel mitochondrial donation techniques.[3]

The Academy warmly welcomes the progress that the Department of Health (DH) has made in drafting regulations for permitting mitochondrial donation techniques to be introduced in clinical trials, and also the opportunity to comment on these regulations at an early stage in this consultation.[4] Considerations of the questions raised in the consultation are provided below. We have focused on responses to research-related questions. These questions were submitted via the DH's online questionnaire.

Question 1: the removal or insertion of nuclear DNA involved in mitochondrial donation.

We agree with the text in the draft regulation that describes this process, as a way of ensuring that transfer of nuclear DNA does not exclude important organelles closely associated with the nucleus.

Question 2: allowing for the transfer of spindles or pronuclei into eggs or embryos with all nuclear DNA removed.

We believe that the regulations should allow for mitochondrial donation techniques that are intended only to transfer all nuclear DNA between eggs or embryos of donors and recipients of treatment. There are techniques available to ensure that all nuclear DNA has been removed from eggs or embryos that would be used in mitochondrial donation treatments.

Question 3: the role of the HFEA in assessing the application of techniques on the basis of individuals' risk of transmitting serious mitochondrial disease to offspring.

In our response to the HFEA's consultation, the Academy supported the notion that if the mitochondrial donation techniques were permissible in trials, prospective mothers should be allowed to choose whether or not to receive either of the techniques as a treatment or choose from the range of other reproductive options available (such as pre-implantation genetic diagnosis, oocyte donation or adoption).[5] These decisions would be subject to all safety and efficacy requirements and we envisaged that mitochondrial donation treatments could only be permitted after comprehensive consultation with clinicians with relevant expertise on these options. We take this stance because it would seem to be very difficult for a regulator to anticipate which types of mitochondrial DNA disease can be deemed 'serious', and the likelihood of offspring suffering from these, for each case under review using existing predictive technologies. Nonetheless, we also recognise the importance of safeguarding patients from the promotion of mitochondrial donation

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[3] The Academy of Medical Sciences (2012). *Statement on mitochondrial diseases.* http://www.acmedsci.ac.uk/more/news/statement-on-mitochondrial-diseases/

[4] Department of Health (2014). *Serious mitochondrial disease: new techniques to prevent transmission.* https://www.gov.uk/government/consultations/serious-mitochondrial-disease-new-techniques-to-prevent-transmission

[5] The Academy of Medical Sciences (2012). *The Academy of Medical Sciences' response to the Human Fertilisation & Embryology Authority's public consultation on mitochondria replacement.* http://www.acmedsci.ac.uk/download.php?f=file&i=13428

services by private-sector services where the approach may not be necessary or appropriate. We acknowledge that the HFEA is effective and well positioned as a regulator to provide this safeguarding. If the HFEA is to assume this role, we would emphasise that significant scope for uncertainty in interpreting prospective mothers' risk of transmitting 'serious' mitochondrial disease should be adopted by the regulator when determining its criteria for assessing applications. This should be done initially on a case-by-case basis. Serious diseases – emerging either at a young age or those considered degenerative in older age—are sometimes erroneously not attributed as mitochondrial in origin (i.e. due to a mtDNA mutation). The regulator should use its power to seek advice from geneticists with specialist knowledge of mitochondrial DNA disease to improve its ability to predict risk of serious disorders arising.

If the treatments become routine over time, and risk-benefit calculations can be revised based on empirical evidence, the role of the HFEA in regulating applications could be reviewed to consider transferring assessment of risk to licensed clinics and individuals seeking treatment. We hope that any regulations do not involve any unnecessary delays for mothers wishing to use these techniques.

Question 4: licensing clinics to undertake mitochondrial donation techniques.

We agree with the position described in the draft regulations that would require clinics to apply to the HFEA for a licence to be able to provide mitochondrial donation treatments.

Question 5: the status of egg or embryo donors for mitochondrial donation.

We stated in our response to the HFEA's public consultation that in terms of the biological contribution that mitochondrial donors provide to offspring, bone marrow donation, which leads to the presence of third-party genes in some of the recipients' tissue, may be a more analogous comparison than gamete donation.[6] Thus, we are supportive of the position described in the draft regulations, where donors of eggs or embryos for mitochondrial donation treatments are regarded in a similar way to organ or tissue donors.

Question 9: other considerations.

The Academy has previously emphasised the importance of conducting long-term and trans-generational follow-up of any offspring born using mitochondrial donation techniques and other assisted reproduction technologies (ARTs), to confirm the long-term safety and efficacy of these treatments.[7] We agree that the regulations should not dictate that the consent for participation of ART recipients in follow-up research is a requirement of permitting treatments. However, there is a strong need for the HFEA to identify and encourage the optimal methods to promote the enrolment of all recipients of mitochondrial donation treatments and their offspring in follow-up studies. Furthermore, we would strongly recommend that the HFEA produces standards for clinics to

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[6] The Academy of Medical Sciences (2012). *The Academy of Medical Sciences' response to the Human Fertilisation & Embryology Authority's public consultation on mitochondria replacement.* http://www.acmedsci.ac.uk/download.php?f=file&i=13428

[7] The Academy of Medical Sciences (2012). *The Academy of Medical Sciences' response to the Human Fertilisation & Embryology Authority's public consultation on mitochondria replacement.* http://www.acmedsci.ac.uk/download.php?f=file&i=13428

conduct evaluations of treatments and promote the involvement of patients in these evaluations, along with the reporting of follow-up data to the HFEA. We would expect that the conditions of licensing clinics to use the treatments would include satisfactory plans by clinics to meet these standards. We are pleased to see that the Department of Health also takes this view, as specified in paragraph 2.40 of the consultation document. We would also like to suggest that the Health Research Authority should also have a key role in facilitating trials to introduce mitochondrial donation techniques.

This response was prepared by Dr Dylan Williams (Policy Officer) and informed by the Academy's Fellows. For further information, please contact Dr Williams (dylan.williams@acmedsci.ac.uk; +44(0)20 3176 2167).

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