

Clones and Three-Parent Babies: the Ethics of Mitochondrial Replacement

A briefing paper and guidance on the consultation questions

The Government has commissioned a consultation to ask people what they think about allowing two possible techniques for creating genetically modified embryos in the laboratory. The newspapers have called such proposals “three parent IVF”; however, this term really only applies to one technique. The other technique they are considering is a form of cloning from one embryo, using a second, donor embryo to create a third, clone embryo. Only the third embryo would survive to be born.

With either technique, this would be the first time UK scientists were permitted deliberately to alter the genome that would be passed on to future generations. In many countries it is illegal to attempt to alter the “germline” in this way. The Government is essentially asking you whether you wish to see genetically modified babies born in the UK.

Currently scientists are asking about only one kind of disease, mitochondrial disease, which is passed by women to their children via genes outside the nucleus of the egg. However, if alteration of the germline is allowed for mitochondrial disease then it will certainly be requested for other diseases. Now is the moment when we decide about the principle: Do we want genetically modified children?

Here is a description of the two techniques about which the Government is asking (you may also wish to look at diagrams on the HFEA website at <http://mitochondria.hfea.gov.uk/mitochondria/what-is-mitochondrial-disease/new-techniques-to-prevent-mitochondrial-disease/>).

- MST (maternal spindle transfer) takes place before IVF. The spindle, which carries the genes in the nucleus of the egg, is removed from the healthy donor egg and replaced by a spindle taken from the egg of the commissioning mother (the woman at risk of passing on mitochondrial disease). All other parts of the donor egg, including the healthy mitochondria, are left in place. The combined egg is then fertilised by the father’s sperm and the embryo has three parents: the spindle mother, the egg donor mother, and the father. Genetic parenthood is complete in the case of the father, but fragmented in the case of the two mothers.
- In PNT (pronuclear transfer) two embryos are created by IVF, one the embryo of the commissioning woman, who will have its mother’s affected mitochondrial genes, and the other the healthy embryo of an egg donor. The embryos are then combined using a technique somewhat similar to the cloning of Dolly the Sheep (the licence for the experiment was adapted from the licence originally given for Dolly-style cloning – see <http://www.hfea.gov.uk/1564.html> and <http://www.theyworkforyou.com/wrans/?id=2011-10-19a.72.1&s>). At the one-cell stage, the donor embryo’s pronuclei containing the nuclear genes are removed, killing that embryo. The partially-gutted donor embryo with its healthy mitochondria is then used to form a new embryo when the pronuclei “harvested” from the commissioning woman’s embryo are inserted. Harvesting the pronuclei from the commissioning woman’s embryo kills that embryo.

- Effectively the commissioning woman's embryo is cloned when that embryo's nuclear genetic material is placed in the partially-gutted embryo of the other woman. To call PNT "three parent IVF" overlooks the fact that it involves three or four original parents conceiving two IVF embryos: embryos who are then destroyed in the process of cloning a third embryo. At the point when the third embryo is created, there is no fertilisation and no eggs or sperm are involved: the embryo is constructed solely from parts of the two earlier IVF embryos. PNT is better described as "embryo creation by destructive embryo cloning", though like other clones the child resulting will contain genetic material from "ancestors" of some kind (not just the two embryos used, but the couple who conceived the first embryo, passing on nuclear genes to that embryo and thus to the clone, and the woman who conceived the second embryo, passing on mitochondrial genes to that second embryo and thus to the clone).

It is important to realise that neither "three parent IVF" (MST) nor "destructive embryo cloning" (PNT) is a treatment for disease. They would not treat mitochondrial disease in any child or adult. Rather, they would allow couples to use either the healthy egg of another woman, or her healthy embryo, so as to retain the good mitochondria, without passing on that woman's nuclear genes or those of the embryo she has donated.

When an egg donor is used in standard IVF, this avoids passing on mitochondrial disease. What is new in MST or PNT is that the donor egg or donor embryo would be genetically modified in an attempt to erase the identity of the egg donor mother (in the case of MST) or the donor embryo (in the case of PNT). The child resulting, even if healthy, would be no more healthy than children conceived using standard egg donation.¹ Moreover, the child would be at greater physical risk from the new procedure, and might well have more serious problems of identity, particularly in the case of PNT where the child is constructed from other embryos used and destroyed for their parts. These techniques cross an important ethical line for no good medical reason.

[Guidance on consultation questions follows.]

¹ From a Catholic perspective there are profound ethical problems with the use of donor gametes and indeed with all non-sexual conception, but this consultation concerns what is *new* about proposals such as "three parent IVF".

The Government has commissioned the Human Fertilisation and Embryology Authority (HFEA) to ask people what they think of MST and PNT. There is more information about these techniques on the HFEA website, where you will also find a link to the consultation questions:

<http://mitochondria.hfea.gov.uk/mitochondria/have-your-say/>

Consultation questions (in red)

It is best to answer in your own words, and a short answer giving your main concern is usually the best approach. Please see below for some things to consider (in black) when composing your answers to the 7 consultation questions.

1. Permissibility of new techniques

Having read the information on this website about the two mitochondria replacement techniques, 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.

THINGS TO CONSIDER:

1. This is where you should say why you think MST (three parent IVF) and PNT (embryo creation by destructive embryo cloning) should not go ahead. Be clear on the reasons why both are morally wrong.
2. MST is making embryos from the eggs or sperm of three people. PNT uses eggs or sperm from either three or four people (depending on whether the donor embryo is made using sperm from the commissioning couple or a donor).
3. PNT is ethically worse because it is reproductive embryo cloning: cloning from one embryo, using a second embryo, minus its own pronuclei, to provide the bulk of the cell, to create a third, clone embryo.
4. PNT is ethically worse because it involves creating and destroying two human embryos.

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?

THINGS TO CONSIDER:

1. Any change will affect future generations in ways that are impossible to predict.
2. This is a dangerous step that is illegal in many other countries for good reasons.
3. Once this is done for one disease it will be done for other diseases and other reasons.

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?

THINGS TO CONSIDER:

1. Both PNT and MST require an egg donor whose egg will be fertilised to create an embryo (in PNT, this embryo is then partially gutted and used to provide the bulk of the cell into which is put the genetic material from the commissioning woman's embryo).
2. Though MST tries to erase the identity of the egg donor mother, the egg will still bear traces of her identity and the child will be able to trace her maternal ancestry through her.
3. If MST is allowed, which it should not be, it should be the children who are born from it who should decide whether they wish to contact their egg mothers. It is patronising to claim in advance that the egg donor mother is not a "real" mother.
4. The attempt to erase the egg donor mother's identity may cause more identity problems for the child, not fewer.
5. In the case of PNT, identity problems may be more severe, as the child will be a clone formed from "spare parts" of two deliberately destroyed embryos.

4. The status of the mitochondria donor

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.

THINGS TO CONSIDER:

1. The egg donor in the case of MST is more than a mitochondria donor. The names maternal spindle transfer and pronuclear transfer show that it is not the mitochondria themselves that are transferred but the *nuclear* genes (the spindle or the pro-nuclei) that are transferred into a second egg or embryo.
2. Existing egg donation does not involve an egg from which many genes have been erased before fertilisation (in the case of MST). Nor does it involve the total replacement of fertilisation by cloning (in the case of PNT).
3. The spindle is not an egg and without an egg there is no embryo. The egg donor is a kind of partial mother, just as the spindle donor is a kind of partial mother.
4. In the case of PNT the egg donor is not the mother directly of the final embryo created, but of an embryo who is destroyed to create that final embryo. This is something potential egg donors may not realise.
5. Many people have concerns about the existing exploitation of egg donors, who may be paid or offered fertility treatment as payment for their eggs. We should not be encouraging this kind of exploitation, particularly in cases where the donor's own genetic child is destined not for birth but for destruction.

b) 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.

THINGS TO CONSIDER:

1. MST and PNT, misleadingly termed “mitochondrial replacement”, should not be permitted.
2. If MST is legalised and children are born, such children should not be deprived of knowledge of the egg donor mother. They should have no fewer rights than other children conceived using donor eggs or sperm.
3. In PNT there will be up to four parents involved in the conceiving of the original two IVF embryos. The PNT child will then be a clone made from these two embryos, who are killed in the process. However, its mitochondrial DNA will be derived from the egg donor, via the second, donor embryo. Given his or her likely state of parental confusion, any child born from this destructive procedure should, at very least, be offered full knowledge of the woman who donated the second egg and of the man whose sperm was used to create the donor embryo with that second egg (if this man is different from the child’s social father).
4. By only allowing one box to tick, this consultation does not allow those opposed to these techniques adequately to express a view about how to mitigate the bad effects.

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.

THINGS TO CONSIDER:

1. MST and PNT, misleadingly termed “mitochondrial replacement”, should not be permitted.
2. History has shown that, if such techniques are legalised, the regulator will not be an effective safeguard against ever-expanding use of the techniques. The only practical safeguard is a clear rule as to which techniques are prohibited. Such rules are best set by Parliament, not by the regulator.
3. By only allowing one box to tick, this consultation does not allow those opposed to these techniques adequately to express a view about how to mitigate the bad effects.

6. Should the law be changed?

In Question 1, we asked for your views on these techniques. 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? You may wish to address the two techniques separately.

THINGS TO CONSIDER:

1. For reasons stated above, MST and PNT should not be permitted and the regulations should not be created to allow them.
2. PNT is much worse than MST for a number of reasons, because it involves cloning and destroying embryos. So if the government is determined to permit “mitochondrial replacement” - which we believe would be a serious error - at least it should not permit PNT.

7. Further considerations

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

THINGS TO CONSIDER:

Both techniques are forms of laboratory conception that use an egg donor at some point of the process. Neither MST nor PNT would be safer or more efficient than standard egg donation, nor would they do any more than standard egg donation to prevent the transmission of mitochondrial disease (which does not happen with standard egg donation), nor would they avoid the need for an egg donor (an egg mother, in the case of MST). The aim of MST and PNT is to satisfy the wish for a genetically related child, and this wish does not justify cloning, embryo destruction, genetically modifying the child or altering the germline.