



Should Australia Allow Mitochondrial Donation?

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Is there any ethical reason why legislation should prevent the use of donor mitochondria in cases where children are likely to inherit mitochondrial disease from their mothers?

The transfer of a donor's healthy mitochondria into a woman's egg or early embryo aims to prevent a child from inheriting mitochondrial disease from its mother. In February 2015 the United Kingdom became the first country to allow the technique, and last month the US Institute of Medicine also determined that mitochondrial donation is acceptable in some circumstances.

Current laws and regulations in Australia are unlikely to allow this treatment to be used clinically so that children can be born with donor mitochondria. However, in all states and territories (except Western Australia), undertaking embryo research into at least some methods of mitochondrial donation may be possible under an appropriate licence.

So far, no such licences have been granted. There are also no plans to review these laws, with the most recent review in 2011 rejecting any change to allow mitochondrial donation.

Should Australia now follow these overseas developments?

Mitochondrial Disease

Mitochondria are organelles within our cells that are responsible for energy generation. It's thought that they originated in bacteria but now exist in our cells in a symbiotic relationship.

Mitochondrial disease occurs when these mitochondria don't work properly. These diseases take many forms but often they affect energy-intensive body parts such as the brain, liver or heart. Mitochondrial disease is debilitating, is often fatal, and at present there's no cure.

Many mitochondrial diseases are caused by problems in the DNA of the mitochondria themselves, which is separate from the DNA found in a cell's nucleus. Mitochondria are only passed on via the mother; a pattern known as matrilineal inheritance. This means that a man with mitochondrial disease will not pass it to his children. Whether a woman passes it to her children depends on the balance of healthy and mutated mitochondria in her egg cells.

Mitochondrial DNA is also prone to developing new mutations. This makes it hard to predict reliably whether and how someone will be affected by mitochondrial disease.

Mitochondrial replacement is proposed as a way of preventing disease from being passed from mother to child. One technique, maternal spindle transfer, removes the chromosomes from an egg cell with damaged mitochondria and inserts them into a donated egg that has healthy mitochondria. This egg is then fertilised and implanted in much the same way as standard in vitro fertilisation.

Another technique, pronuclear transfer, transplants the nuclei of a sperm and egg (together termed the “pronuclei”) from an embryo created by the parents to an early embryo created using the father’s sperm and a donated egg that has had its own pronuclei removed.

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Both techniques will result in an embryo that has nuclear DNA from the mother and father, and mitochondria from a donor. Any child created would be genetically linked, through mitochondrial DNA, to an egg donor as well as to his or her main genetic parents – hence the expression “three-parent IVF”.

“Three-Parent” IVF?

Should it matter that a child has three biological parents? The first thing to think about here is whether mitochondrial donors are really a “parent”. While the children created will be genetically linked to the donors, it’s far from clear that this link is sufficient to make them parents.

Only around 0.1% of our genes are contained in mitochondria (the other 99.9% is in the cell’s nuclei), so the donor only provides a tiny fraction of the child’s genetic material. That said, this DNA is important: it determines the difference between health and illness. It’s also present in thousands of copies per cell, while there are only two copies of each gene in the nucleus.

We can also ask whether there’s really anything bad about children having a biological link with three people. There are already lots of families that only exist because of the biological input of a third person, such as children created using traditional egg donation or through surrogacy. In the case of egg donation, for example, the child’s “social mother” becomes pregnant and gives birth to her child but she is not genetically related to her baby because the egg came from a donor.

Thus it’s not clear that “three parent IVF” (if that’s what mitochondrial donation is) would be all that different from practices that we already accept.

Genetic Modification

Another concern is that mitochondrial donation is a kind of genetic modification that will affect future generations. This has ethical relevance as it could permanently change the gene pool. Some people are concerned that this sort of genetic modification is too dangerous due to the unknown nature of its effects (e.g. the US Institute of Medicine recommends that this technique be used only to implant male embryos to avoid passing on donor mitochondria). Others object to it because they think it is wrong to “interfere” with human nature to this extent.

But against this, it could also be argued that mitochondrial replacement isn’t really modification. Donated mitochondria are naturally occurring (in the donor’s egg) and not engineered or manufactured.

There is also no change at the level of DNA; rather, it involves the substitution of one set of mitochondria for another. This means that we’re using genetic material that already occurs in nature, not adding anything new or artificial. According to this view, mitochondrial replacement is more like an organ transplant than like genetic engineering.

Furthermore, many different policy decisions have major effects on those yet to be born, such as decisions about the environment and climate change, or whether to go to war. Mitochondrial replacement is not unique in affecting the future and, given the small numbers involved – around one in 5000 people will develop serious mitochondrial disease – its effects may be quite limited compared with other things that we do.

The Ethics of Safety and Risk

In the UK, a high-level scientific review committee deemed mitochondrial donation safe enough to proceed to clinical use. However, this doesn’t guarantee that this treatment will be risk-free. Debates are ongoing in the scientific literature about what effects might occur as a result of mitochondrial transfer. Some worry that data from experiments in species such as mice and fruit flies, in which swapping mitochondria had untoward effects, have been overlooked. Others argue that these data are not transferable to humans or are being over-interpreted.

From an ethical perspective, the key issue is how we should decide on the acceptable level of risk for mitochondrial donation. Sometimes a precautionary approach can be taken, in which the use of a new technology is limited until serious risks are known to be minimised. However, this can lead to long delays. It is also important to keep in mind that the main alternative for these families – having a child affected by mitochondrial disease – is so bad that a certain level of risk is justified in order to prevent this suffering.

Is Mitochondrial Replacement Unnecessary?

Some have also argued that we shouldn't allow mitochondrial replacement because it's not needed. The argument here is that affected parents already have other options so there's no need to develop mitochondrial replacement. For example, Canadian bioethicist Françoise Baylis argues that:

women at risk of having children with mitochondrial disease can have their own children using much less risky alternatives. For example, they can make a baby the old fashioned way, have prenatal diagnosis and, if the fetus is affected, they can choose to have a termination of pregnancy. Alternatively, they can make an embryo using IVF and have preimplantation genetic diagnosis... They can have IVF and egg donation or embryo donation. They can choose to adopt a child. Using one or other of these options, women can become mothers without putting their future children in harm's way with the use of mitochondrial replacement technology.

While these are all potential options, prenatal diagnosis or preimplantation genetic diagnosis are not possible for many couples who are at risk of passing on mitochondrial disease. If a woman's eggs have mainly or only mutated mitochondria, then any child born from one of those eggs will have the same high level of mutation. No amount of selecting is going to change that.

And finding a suitable egg donor or adoptive child isn't easy. In 2013, only 406 babies were born from egg donation in Australia – a fraction of the 300,000 or so children born that year. Australian couples seeking egg donation also often travel overseas to find a donor, prompting the Australian Health Ethics Committee to propose legalising payment for egg donors here. Additionally, the most recent adoption statistics for Australia show that there were only 317 adoptions in 2013–14. Of these, only 12% of adoptions involved children under 12 months of age.

It is also apparent that – in common with many other families – couples at risk of passing on a mitochondrial condition attach value to the genetic link between parent and child and would very much like to have children who are both genetically “theirs” and free from mitochondrial disease.

A Right to Know?

Australian guidelines state that “persons conceived using ART procedures are entitled to know their genetic parents”. This raises the question of whether mitochondrial egg donors should be considered as “genetic parents” for these purposes. It also raises the question of whether children created as a result of mitochondrial donation should have a right to know who the egg donor was.

However, it might also be argued that mitochondrial donors aren't biological parents because their genetic contribution is so limited and that – unlike “regular” egg and sperm donors – children created via mitochondrial donation won't inherit their donors' most important personal characteristics, which pass via cell nuclei.

If donor information can be stored without imposing huge costs on clinics and without putting off too many donors, a case can be made for storing information about mitochondrial donors with a view to releasing this when the children created reach maturity. Those who don't want to access this information needn't do so, but some may have a strong desire to know more about their origins and may be frustrated or distressed if information is withheld.

Thus it may be best to err on the side of caution and to retain donor information for those who want it.

Moving Forward, Cautiously

It's too early to say whether mitochondrial replacement techniques can be developed that are sufficiently safe and effective for widespread clinical use. As with any new medical treatment, thorough evaluation and research is needed. There is, however, no conclusive ethical argument against proceeding with this research. In addition, given the importance to many people of having a child who is both genetically “theirs” and free from mitochondrial disease, there's a strong case for allowing it to proceed, provided that there's rigorous regulation and monitoring.

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