



## CNA Commentary

# With UK success, should Singapore reconsider 3-parent IVF?

Eight babies in the UK have been born with DNA from three people. NUS Centre for Biomedical Ethics' G Owen Schaefer considers whether Singapore should revisit the possible benefits – and pitfalls – of mitochondrial replacement.

**By Owen Schaefer**

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SINGAPORE: The normal course of human reproduction involves two biological parents - a mother and a father. But in the United Kingdom, eight babies have been born with DNA from three people, scientists from Newcastle University reported recently.

It's the result of an in-vitro fertilisation technique called mitochondrial replacement. Some call it "three-parent IVF". The procedure was developed to help women who are carriers of mitochondrial disease - which is passed down from mothers to their offspring - have healthy children.

Mitochondrial diseases, estimated to affect 1 in 5,000 births, can cause a variety of serious health problems. These include stroke-like episodes, seizures, hearing loss, diabetes and deterioration of brain functioning.

In 2021, Singapore's Bioethics Advisory Committee (BAC) recommended against permitting mitochondrial replacement, citing uncertainty around the safety of the technology. The committee recommended waiting for better data.

"A more definitive discussion of these issues would be better undertaken at a future date when more certainty regarding the science, techniques, safety and efficacy ... is available," stated the BAC's interim report.



With Newcastle reporting healthy births and Australia already paving the way to allow mitochondrial donation, is it time to reconsider?

Such consideration should be in full view of a variety of ethical and social issues.

## **WHAT IS MITOCHONDRIAL REPLACEMENT?**

Mitochondria are tiny parts of cells that act like batteries, storing and generating energy necessary for cells to operate. Mitochondrial defects can be particularly problematic for the functioning of brain and muscle cells, leading to brain disease or severe muscle weakness.

The Newcastle researchers used a method called “pronuclear transfer”. It involves three people: the mother, the father and a donor.

Doctors begin by fertilising both the mother’s and a healthy donor’s eggs with the father’s sperm. From the mother’s fertilised egg, they remove the nuclear DNA - which determines most of a person’s traits - leaving behind the unhealthy mitochondrial DNA. Then, they remove the nuclear DNA from the donor’s fertilised egg and replace it with the nuclear DNA from the mother and father. The donor’s healthy mitochondria stay in place.

The resulting egg - now carrying the parents’ nuclear DNA and the donor’s healthy mitochondria - is then implanted into the mother. Babies born from the process inherit 99.9 per cent of their DNA from the parents and 0.1 per cent from the donor.

## COMPLICATED QUESTIONS

The idea of “three-parent babies” raises difficult questions. Some people are uneasy with it; the science sounds unnatural to them. Others have raised objections grounded in their faiths, such as disruption to a child’s lineage or altering and destroying embryos.

Another concern is that the risks simply aren’t worth the benefits. The BAC report flagged key questions: What if the faulty mitochondria aren’t fully removed? What if new mutations emerge and jeopardise the welfare of future generations?

The Newcastle results partly address these worries, but it’s just one study and the sample size is small. Caution is still warranted.

At the same time, there is a positive ethical case worth highlighting.

First and foremost, it can prevent the transmission of harmful disease. Children wouldn’t inherit painful, life-shortening diseases. Women who carry mitochondrial disease could still have biological children without passing on illness. As a result, the number of cases of mitochondrial disease in a population would be reduced.

It also gives parents more options, especially women who want children genetically related to them or do not want to use a full egg donor or adopt.

## IS IT WORTH THE COST?

Even if the science is sound and the ethics can be worked through, there’s still the matter of cost.

Only a small number of people would benefit from mitochondrial replacement. The Newcastle study’s small sample size is not an accident. In Singapore, there isn’t a definitive analysis of how many families might benefit, but the number is likely to be low.

Significant resources would be needed to run an effective, safe and responsible mitochondrial replacement programme. This includes conducting public consultations, potential legal reforms, hiring experts and practitioners, conducting preliminary research and establishing infrastructure.

A question may be raised whether such resources are justifiable when the number who could benefit is small.

Ultimately, these questions of science, ethics and cost require further societal consideration. But at the very least, the Newcastle results should prompt Singapore and other countries to (re)start a conversation around mitochondrial replacement. Do we remain cautious and wait? Or do we take careful steps forward?

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