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Three-person IVF trial 'success'

By Michelle Roberts Health editor, BBC News online



Safety studies are still needed

US scientists say a human and animal trial of a controversial new IVF treatment has yielded promising results.

The findings in Nature magazine show healthy-looking embryos can be created from a mix of three adult donors.

Human embryos were grown in the lab and some appeared normal, while monkeys born using the same technique remained fit and well, now aged three.

A public consultation on the ethics of using this IVF in the UK is under way.

Its findings will be reported to the health secretary in spring 2013.

The technique is designed to prevent debilitating and fatal "mitochondrial" diseases, which are passed down only from mother to child and which cause muscle weakness, blindness and heart failure.

"It is still a long way off ready for human use"

Prof Peter Braude King's College London

By using two female egg donors, these DNA errors could be cancelled out, scientists believe.

Three-person IVF uses the core genetic information from mother and father as usual, but puts it into a donor egg which contains healthy mitochondria.

Mitochondria sit in the cytoplasm of the egg - akin to the white of a hen's egg. They contain only a tiny fraction of our genetic material, with the bulk that determines things like our hair and eye colour housed in the nucleus - a speck in the yolk if you use the hen's egg analogy.

Scientists have been studying two ways of creating three person embryos.

One way is to take the nucleus from the mother's egg and put it into a donor egg that has healthy mitochondria and has had its own nucleus removed. This new egg can then be fertilised with the father's sperm.

Another way is to fertilise the mother's egg first before removing the nucleus and putting it into the donor egg.

The latest study looked at the first method.

Testing

The Oregon Health team took eggs from seven women who had volunteered to take part in the research.

"The question is which method will work best in humans? Neither the US nor Newcastle researchers has allowed any human embryos to be implanted - all were destroyed after just a few days when still smaller than a pinhead."

The scientists were able to replace the mitochondrial DNA in 65 of the eggs and then looked to see how well these fared over the next week or so.

The fertilisation rate afterwards was similar to the 33 control eggs that had not been manipulated, although over half had abnormal qualities.

Those that did fertilise normally developed to blastocyst stage - five or six days later, the point at which IVF embryos are normally transferred into the mother's womb - at a similar rate to the controls.

Dr Masahito Tachibana and colleagues say their research shows that the technique can work, at least in the lab. It is still not clear if it could lead to a healthy baby.

The scientists now want to be able to do more studies to ensure the treatment is also safe.

UK expert Prof Mary Herbert, of Newcastle University, has also been studying three person IVF, but using the other method which takes the nucleus out of an already fertilised egg.

She called the latest findings "encouraging" and said they were further proof that the concept was sound, although she believes the technique she uses will provide better results.

Review

Before either method could be used to help couples have a healthy baby in the UK, the government would need to give its approval and any clinic would need to obtain a license from the regulator - the Human Fertilisation and Embryology Authority (HFEA). Similar approval would be needed in other countries.

Last year the HFEA was asked to review the scientific effectiveness of both techniques. That review panel decided that the two methods might be

useful in preventing mitochondrial disease, but asked for further experiments to assess their safety.

Prof Peter Braude, Emeritus Professor of Obstetrics and Gynaecology, King's College London, said: "It is exactly the sort of science that the HFEA expert committee recommended needed doing, and demonstrates further the feasibility of this technique.

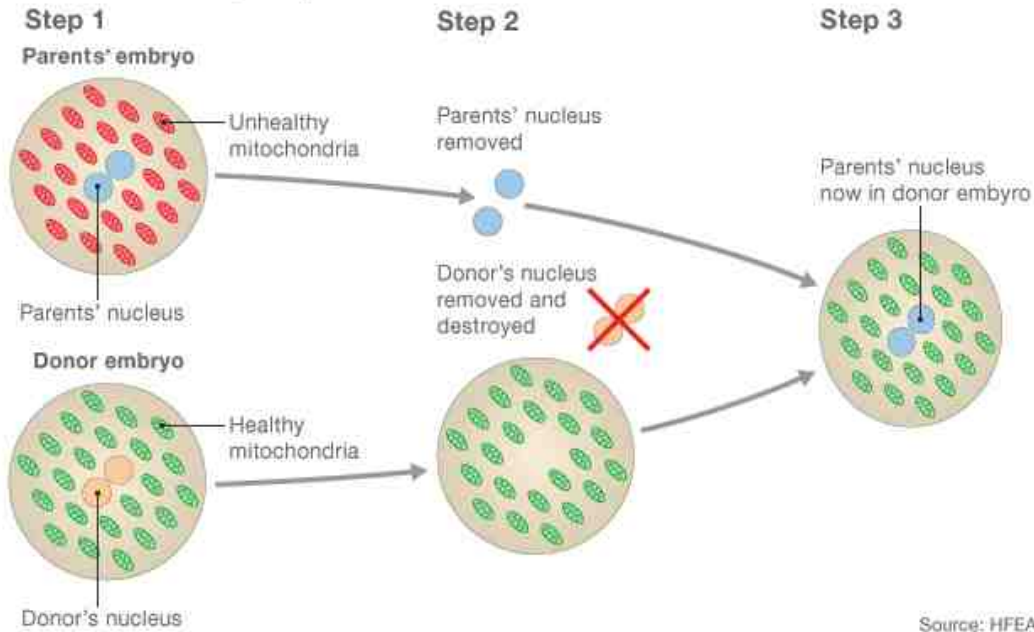
"However it is still a long way off ready for human use."

He said: "Only one in five of the original eggs obtained fertilised normally and made it through to the implantation stage.

"This would mean that in order to be certain of getting embryos that might be suitable for transfer, around 12 eggs might be needed, not always possible in an IVF procedure."

How do you make a baby from three people?

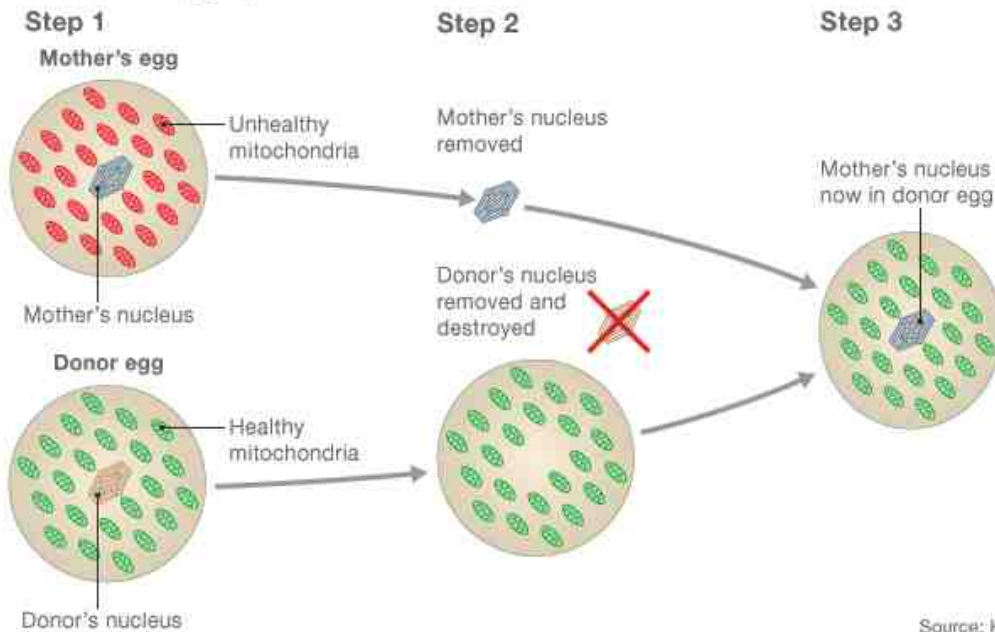
Method one: Embryo repair



Source: HFEA 1) Two

embryos are fertilised with sperm creating an embryo from the intended parents and another from the donors. 2) The pronuclei, which contain genetic information, are removed from both embryos but only the parents' is kept 3) A healthy embryo is created by adding the parents' pronuclei to the donor embryo, which is finally implanted into the womb

Method two: Egg repair



Source: HFEA

Step 1. Eggs from a mother with damaged mitochondria and a donor with healthy mitochondria are collected. Step 2. The majority of the genetic material is removed from both eggs. Step 3. The mother's genetic material is inserted into the donor egg, which can be fertilised by sperm.

Ethics of using three people's DNA to create one baby



Every so often a medical technique comes along of fundamental significance to medicine and society.

Transplantation and IVF are two examples. The first gave the chance of prolonged life to patients with failing organs. The second the chance of parenthood to couples with fertility problems.

Mitochondrial replacement might seem obscure by comparison. Unlike transplantation and fertility treatment, it would benefit very few couples. Those it could help would be able to have healthy children free of a potentially fatal genetic disease. Future generations of those families would also be free of the genetic fault.

But it also has huge potential significance for society because for the first time children would be born with DNA from three people - what has frequently been dubbed 'three-parent IVF'.

Crucially that genetic alteration to what's known as the germ line, would be permanent, handed down from generation to generation.

That's why a consultation begun today by the [Human Fertilisation and Embryology Authority \(HFEA\)](#) is so important.

My colleague [James Gallagher has written](#) about the techniques involved in mitochondrial replacement.

I will give just a brief explanation.

About one in 200 children is born with a fault in their mitochondria - these are the power packs outside the nucleus of each cell.

Most have mild or no symptoms but a minority suffer devastating effects which can include muscle weakness, neurological, visual and hearing disorders and heart disease. These can be progressive and fatal.

What's more that genetic fault is passed on down the generations, via the maternal line from mother to child.

My report from April 2010

[Two years ago scientists in Newcastle reported](#) that they could fix the problem through IVF technology.

The key was to replace the faulty mitochondrial DNA which they did by using the healthy mitochondrial DNA from a donated egg.

The resulting embryo contains all the genes from the nucleus of the parents (more than 20,000) plus a few dozen genes from the donated mitochondrial DNA.

The team, led by Prof Doug Turnbull, created 80 embryos but none was transplanted into a woman.

A scientific review last year concluded that there were no safety concerns which should prevent the technique from being used to help couples. But it recommended further research to explore the issues, which is currently under way in Newcastle.

Case study

Sharon Bernardi's son Edward died last year aged 21. He had Leigh's disease, a rare progressive mitochondrial disorder that affects the central nervous system. He needed constant care through his life. All her other children died within days of birth as a result of the inherited condition.

Sharon, from Sunderland, said: "Losing one child is bad enough but I lost six babies to mitochondrial disease. Edward suffered a lot towards the end of his life and was in terrible pain. I hope other couples will be allowed to have this new treatment and be spared what my husband and I went through."

Which leaves the ethical concerns. The technique raises many issues: what is the legal status of the woman who donates her DNA? How might any child that is born feel about having DNA from three people? When should they be told?

But this is not just an issue for the couples involved. For the first time it will mean that scientists are altering human genetic inheritance.

The addition of a tiny amount of DNA from a third person will be passed down the germ line - through the eggs - to subsequent generations.

Prof Lisa Jardine, the Chair of the HFEA said she expected some strongly-held views on the subject.

"This is an area that generates extreme opinions like almost no other issue except assisted dying. That is not a surprise since they are about taking and

creating life."

Prof Jardine said that it would ultimately be up to the health secretary to rule on whether the technique should proceed to the clinic. This would not require an Act of Parliament but there would need to be a debate in both Houses of Parliament.

The consultation runs until 7 December and details can be found on the [HFEA website](#).