



FDA considers controversial fertility procedure. What's at stake?

BY NITA FARAHAANY, February 25, 2014

On [Tuesday Feb. 25](#) and [Wednesday Feb. 26](#), the FDA will consider a controversial cutting-edge fertility procedure otherwise known as “oocyte modification in assisted reproduction for the prevention of transmission of mitochondrial disease or treatment of infertility.” Despite the [hype](#), the mitochondrial transfer procedures being considered are far from the “creation of three-parent babies.”

Instead, the FDA is finally considering whether it should green-light small clinical trials that could one day enable the thousands of women afflicted with mitochondrial disorders to have a shot at having healthy genetic children. Passions tend to run high in this area. Before the alarm bells start ringing on both sides, it might be helpful to have an overview of what is and is not at stake.

What's at issue?

1. What are mitochondria?

Every cell in the human body has a nucleus, where about 98 percent of your DNA resides. But about 2 percent of your DNA is inherited solely from your mother, which is known as the mitochondrial DNA. The easiest way to think of this is to visualize a cell, with its small nucleus inside in a little packaged bundle, and the mitochondria in the free-floating fluid surrounding that bundle. Because sperm cells lose their mitochondria when they fertilize an egg, all of the mitochondria we have are passed onto us from our mothers' egg.

Mitochondria make energy. They produce more than 90 percent of the energy that our bodies need and play a critical role in regulating cell energy and cell growth. [Here](#) is a very nice and detailed explanation.

2. What are mitochondrial disorders?

Inherited mitochondrial disorders are progressive disorders that cause debilitating and disabling health problems. Because mitochondria are inherited solely from the mother, an affected mother will pass on mitochondrial abnormalities to all of her children. There is no cure for these conditions, and they can result in the death of babies, children and young people.

3. How many births are affected by mitochondrial disorders?

About one in 5,000 births and likely an even higher proportion of fetuses that never make it to birth have a mitochondrial DNA mutation. Mutations in mitochondrial DNA can cause rare but serious illnesses and defects, including heart failure, dementia and blindness; and many of these conditions are fatal. While the severity and onset of symptoms vary, mitochondrial diseases tend to affect tissue with high-energy demands, such as the heart, muscle and brain. There is no way to treat these conditions once acquired, and it is extremely difficult to predict how severely a child will be affected from screening alone.

4. What are the mitochondrial techniques that the FDA is considering?

Scientists have discovered novel ways to prevent the transmission of mitochondrial DNA from a mother to her children. So, if a mother's mitochondrial DNA carries a harmful mutation, these new techniques can avoid the transmission of disease to future generations.

There are several mitochondrial replacement techniques that are currently in development, and researchers have had success with these techniques in both animals and in human zygotes, although they haven't transferred any embryos to a woman to develop into a live birth.

The new techniques under consideration use the mitochondrial DNA from an unaffected egg donor, together with the nuclear DNA from an affected woman. Put simply, the mitochondria of the affected egg are removed and replaced by the mitochondria from the healthy egg. The nucleus of the mother undergoing the procedure remains unchanged but is now fueled by the healthy donor mitochondria.

Because the mitochondria give energy but not the coding traits that make us who we are, what results is a woman's own egg — with healthy mitochondria to support its fertilization by sperm and subsequent growth into a healthy embryo and healthy baby. The technique the FDA will be focused on is called maternal spindle transfer. [Karen Weintraub, over at USA Today](#), has a nice story (thanks for quoting me!) which explains how the leading researcher in the United States, [Shoukhrat Mitalipov](#), at Oregon Health & Science University in Portland, has tested mitochondrial transfer in animal models (monkeys) and is now seeking FDA approval to begin small-scale clinical trials in women with mitochondrial abnormalities.

In this technique, nuclear DNA is removed from the intended mother's egg, and the rest of the egg with the unhealthy mitochondria is discarded. The nucleus from the donor egg is removed, which leaves healthy mitochondria behind. The intending mother's nucleus is transferred into the donor egg, after the donor egg's nucleus is removed. What results is a healthy egg, which can be fertilized by the father's sperm.

5. Is it safe?

That's the main question the FDA is considering. Research is taking place in both Britain and the United States on several types of mitochondrial replacement techniques — including pronuclear transfer (PNT), the maternal spindle transfer (MST) the FDA is considering and nuclear genome transfer (NGT). There have been successful trials in animals, and the successful creation of healthy human zygotes. But to date, there is no reported case of an embryo transferred into a woman for development to know whether it is safe.

Just like in vitro fertilization and other reproductive technologies, there is a small but unknowable risk until we allow small clinical trials to proceed. We have accepted that

risk in the past, when overwhelming scientific evidence gives us confidence to move ahead to small-scale clinical trials. But there is no way to know for sure without permitting some trials to proceed.

6. Have other authorities considered mitochondrial transfer?

The Human Fertilisation and Embryology Authority (HFEA) agency in Britain, which is responsible for oversight of reproductive technologies, did an [in-depth analysis](#) of mitochondrial transfer and advised the British government to permit mitochondrial transfer “so long as it is safe enough to offer in a treatment setting and is done so within a regulatory framework.” They found that the ethical concerns were outweighed by the arguments in favor of permitting mitochondrial replacement, and that it might be unethical to *not* provide parents with the option because of the suffering that this option could mitigate.

Also in Britain, the Nuffield Council on Bioethics examined the scientific, ethical and legal issues surrounding mitochondrial transfer techniques and likewise concluded that given the tremendous individual and social benefits involved, it would be [ethical to proceed](#) with these techniques in clinical trials.

7. If a donor gives mitochondria, is she a parent, too?

In my opinion, no. Embryos that result from these techniques have genetic material contributed from three different individuals, but the mitochondrial donor is not a parent — genetically, or otherwise.

When using mitochondria from a donor egg, the resulting egg (which has the nucleus from the intending mother) has 99.9 percent of its coding DNA from the intending mother. The donor provides the energy necessary for the egg to function normally. When the egg is then fertilized by a sperm cell, the resulting embryo carries less than .1 percent of its DNA from the mitochondrial donor.

8. What about that slippery slope?

As the FDA meetings proceed, you’ll undoubtedly hear and read a lot of fear-mongering claims about “opening the floodgates to designing perfect babies” or arguments that

approving mitochondrial replacement would put society on a slippery slope toward dystopia. These concerns are overblown. In future posts, I'll explain why I believe that as a society, we can safeguard the floodgates when they are threatened. And why those floodgates aren't implicated here.

9. So what should we do?

You can learn more about the pros and cons of mitochondrial transfer by listening to the Intelligence Squared Debate, in which I participated, [here](#). It was a great debate and really aired a lot of the issues.

Check back regularly over the next couple of days, and I'll also give you my current assessment of the hearings and share with you my opinion about how the FDA should proceed. But for now, I thought we should start with a common set of objective facts.

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