Mitochondria Replacement to Avoid Maternal Transmission of Mitochondrial Disease

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Is germ-line gene therapy acceptable in order to avoid maternal transmission of mitochondrial disease? Yes, says the UK's Nuffield Council on Bioethics (NCB) in its report Novel Techniques for the Prevention of Mitochondrial DNA Disorders: An Ethical Review, published in June 2012. In September 2012, the UK's Human Fertilisation and Embryology Authority (HFEA) launched a public consultation on the same issue. Four different germ-line therapy techniques had been proposed by the NCB; the HFEA sought the public's views on two of these: pronuclear transfer and maternal spindle transfer.

The focus of the ongoing ethical discussion reflected in the HFEA consultation is not the risks that might be attached to these procedures, but inter-generational relationships and attitudes toward the child-to-be. The question here is whether these kinds of techniques respect nascent human life and welcome the child-to-be as our neighbor. In order to assist us in thinking about this question from a Christian perspective, I shall sketch the techniques under consideration and, in light of a Christian understanding of human dignity and the value of human life, formulate three principles in terms of which to evaluate mitochondria replacement techniques.

The Four Techniques

Three of the techniques, namely pronuclear transfer, maternal spindle transfer, and blastomere nuclear transfer, lead to the creation of embryos free of faulty mitochondria. The fourth technique, mitochondrial transfer, involves adding healthy mitochondria to an egg before it is fertilized.

Mitochondrial disease can be serious and even fatal. So ways of avoiding maternal transmission of such disease
would be welcome?but not, of course, at any price. What, then, is the price of the techniques under consideration?

Pronuclear transfer and maternal spindle transfer both involve cell nuclear transfer. They are in this respect similar to the cloning technique used to create Dolly the sheep in 1996. In the case of pronuclear transfer two IVF embryos are created. One is the embryo of the intending mother with mitochondrial disease and her partner. This embryo has faulty mitochondria. The other is created from a healthy donor?s egg and sperm, usually from the intending mother?s partner. The donor?s embryo is enucleated?the two pronuclei (genetic material from both the egg and the sperm, which has not yet merged at this stage) of the cell are removed. And then the two pronuclei of the intending mother?s IVF embryo are transferred to the donor?s IVF embryo. The result is a reconstructed embryo containing the pronuclear DNA of the intending parents and healthy mitochondria contributed by the donor.

The technique, then, involves the sacrifice of at least one embryo?the donor?s?and arguably two embryos depending on how one parses the identity conditions of the reconstituted embryo with that of the intending mother?s embryo. It results in a reconstructed embryo with contributions from two genetic mothers: the intending mother and the egg donor; the intending mother and father provide the ?combi-embryo?s? pronuclear DNA, while the egg donor provides healthy mitochondrial genes.

Maternal spindle transfer likewise requires an egg donor free of mitochondrial disease. The spindle of chromosomes (in effect, the cell nucleus) from a healthy, unfertilized donor egg is removed and replaced by the spindle of chromosomes from the egg of the intending mother, a woman suffering from mitochondrial disease. The result of maternal spindle transfer, then, is a ?combi-egg? with the intending mother?s chromosomes and healthy mitochondrial genes. This healthy egg can then be fertilized in vitro, thus allowing the woman with mitochondrial disease to have a baby free of the disease.

No embryo is destroyed in the process, but?again depending on how one parses the identity conditions?at least one egg (the donor?s) is destroyed, and arguably two. The resulting embryo has two genetic mothers, as its nuclear DNA comes from the intending mother and the mitochondrial DNA from the egg donor.

The two other techniques discussed by the Nuffield Council, but not by the HFEA, are blastomere nuclear transfer and cytoplasmic transfer. In the case of blastomere nuclear transfer an egg from the intending mother is fertilized with sperm from her partner. At day five after fertilization, when the embryo has turned into a multi-celled blastocyst, a number of its cells, called blastomeres, are removed. The nucleus of each of these blastomeres is extracted and transferred into enucleated eggs from a donor free of mitochondrial disease. This results in embryos with the intending parents? nuclear DNA and healthy mitochondria from the donor eggs.

Again, the embryos have two genetic mothers. The father of the embryo?or embryos?is the intending mother?s partner. And, as in the case of pronuclear transfer, the technique involves embryo destruction. The many donor eggs are destroyed, and arguably, the intending mother?s original IVF embryo is as well.

In cytoplasmic transfer, the least manipulative of the four techniques, cytoplasm from a healthy donor egg is injected into an egg of the intending mother, the woman with mitochondrial disease. The result is an egg with both healthy and unhealthy mitochondria. The technique has been used to rejuvenate eggs of women with problems conceiving. But it would appear that it does not always yield germline changes in resulting offspring. This technique might therefore be of little use in avoiding maternal transfer of mitochondrial disease. Furthermore, the NCB reports that cytoplasmic transfer ?has been largely discredited in the scientific community because of safety concerns.? So let us say no more about this technique.

Three Christian Guidelines
In the light of Christian understanding of human dignity and the value of human life, I shall outline three principles which might guide us when evaluating pronuclear, maternal spindle, and blastomere nuclear transfer.

We must not treat the child, born or unborn, as if he/she were a mere commodity of only instrumental value to us.

For Christians, every human life is of intrinsic value and so deserves respect and protection. An embryo, like any human being, is a participant in human nature and thus in the image of God, which ensures that she, too, possesses such value. Neither pronuclear transfer nor blastomere nuclear transfer reflects these attitudes towards the human embryo. This is obvious in the case of those embryos that are destroyed. They are treated in a purely instrumental way and seen as no more than raw material to be broken up in order to fabricate the desired products. Nor are the reconstructed embryos treated as human beings possessing intrinsic value. In the case of both pronuclear transfer and blastomere nuclear transfer, the resulting aggregate embryos?and hence the children-to-be?are assembled according to design as manufactured items. They too, then, are treated instrumentally, as are all artifacts (things produced or crafted by human endeavor).

Maternal spindle transfer involves egg destruction and aggregation rather than embryo destruction and aggregation. Nonetheless, the resulting embryo free of disease is an artifact; instead of being received as a gift with intrinsic value, it has been fabricated according to specifications dictated by its perceived purpose. So, not only does the technique reflect instrumental attitudes towards the eggs destroyed, but it also involves an instrumental attitude towards the child-to-be: the child comes into existence in accordance with humanly-established parameters in order to satisfy a certain standard.

There is also the question of egg donation. All three techniques involve egg donation, and, as Oliver O?Donovan noted in his book *Begotten or Made?* to participate in engendering a child for the sole purpose of allocating ?one?fs parental relation to another . . . implicitly converts the child from a person to a commodity.? Whether or not money is involved in the transaction, the child or child-to-be is effectively treated as a possession, not as a person with intrinsic value.

Treat the child as a neighbor and give her an unconditional welcome as a gift from God.

Jesus taught us to recognize and welcome children as our neighbors (Mt 19:13-13; Mk 10:13-16; Lk 18:15-17); this means, among other things, that children possess independent status as ?fully-fledged? human persons with inherent integrity, or completeness. But to come into being as a manufactured entity by aggregation and egg donation in order to satisfy a humanly-established standard is depersonalizing. It is, again, to enter the world as an artifact. As regards pronuclear and blastomere nuclear transfer, both the embryos produced (the children?to-be) and the sacrificed embryos are treated as mere inanimate biological material subject to manipulation. To treat the human embryo and child-to-be this way is to demonstrate a materialistic understanding of human life. On a Christian understanding, human life transcends the material from the moment of conception. It comes from God. It is created in the image of God. And it is meant to return to God. The human birth, life, and death of Jesus bear witness to this.
In the case of both pronuclear transfer and blastomere nuclear transfer, the end-product of the technique is a collage assembled from pieces of previously complete embryos. And in both cases the child-to-be is fabricated with a view to meeting a certain standard. These techniques pursue established parameters of health at the expense of nascent human life. This is not to accept the child-to-be as an intrinsically valuable gift and as it is, with inherent integrity. Neither technique is compatible with the requirement to treat the child as neighbor and as a gift from God, to give him or her an unconditional welcome. Rather, both pursue health at the expense depersonalizing the child.

Nor does the use of maternal spindle transfer satisfy the principle under consideration. This technique involves creating an egg by assembly of genetic material from different eggs, for the purpose of causing that egg to become an embryo created according to humanly-established specifications. Once again, the child-to-be is not treated as a neighbor and gift, and it is not given an unconditional welcome as such.

We should not seek to assume the role of God vis-à-vis our children, but we should serve and love them as servants of God.

A parent, scientist, medical technician, etc. who sees an embryo primarily as mere, or little more than, biological material might well feel he has a right and perhaps even a duty to manipulate this material in order to create a healthy child.

On a Christian understanding, however, there is no such right and no such duty. Christian belief entails humility. As Christians we recognize that there are limits not only to what we can do, but to what we should do as well. Our recognition of the embryo, foetus, and child as our neighbor is incompatible with treating nascent human life as disposable material to mold to our understanding of what a human should be like. Healing a child who is here, whom we regard as a fully-fledged person possessing independent integrity as such, is one thing; making one to specification is another. To do the latter is not to serve our neighbors as servants of the God who is both our and their creator; it is to assume creative power over them ourselves.

In Sum

To manufacture children-to-be by techniques like pronuclear, blastomere nuclear, and maternal spindle transfer is not to welcome and accept children with neighbourly love. When we adopt a perspective in which the costs associated with such techniques are justified for the sake of children-to-be’s conformance to humanly-established standards of health, we fail to regard human persons as such, with all the diversity that entails. We impoverish our society by making it less welcoming of difference and diversity. Before employing the kinds of technology spoken of here, we should ask ourselves if a society characterized by such failure is where we wish our children to live.

References


I have been following Neil Messer’s example of seeking to establish some principles in the light of which to evaluate different practices. See, Neil Messer, Respecting Life: Theology and Bioethics (London: SCM Press, 2011).


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