Is Ooplasm Transfer Safe for the Offspring?

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By Sheldon Krimsky


The first reported human pregnancy following cytoplasm transfer from donor oocytes into a woman’s egg took place in 1997.1 Like many advances in assisted reproduction, ooplasm transfer is designed to help women who seek a healthy pregnancy—a noble endeavor. However, I offer three questions that should be answered before the procedure moves forward to gain FDA approval and possibly becomes institutionalized:

1. Is ooplasmic transfer safe and effective for the offspring?

2. If the procedure is found to be generally safe but with some risks, do prospective parents have the authority to undertake the procedure, balancing risks and benefits, without additional oversight?

3. Are the potential benefits of ooplasm transfer for improving fertility or preventing the transfer of mitochondrial disease unique and sufficient to open the door to germ line genetic modification?

Question 1 is largely scientific; questions 2 and 3 are largely ethical. My remarks today address question 1.

Most scientists who specialize in the biology of reproduction and who have written about cytoplasmic transfer have a clear message.

• Cytoplasmic transfer appears to be consistently associated with mitochondrial heteroplasmy.2
• Heteroplasmy, or babies born with two distinct female mitochondrial genomes, is a risk which must be understood before cytoplasmic transfer aka ooplasm transfer is considered for clinical practice.3
• While an estimated 30 babies have been born using the technique, there have been no systematic follow-up studies that examine the rate and degree of heteroplasmy in the newborn and in cases where it exists on its effect on the developmental health of the child.

A recent review in Pub Med for the terms heteroplasmy and mitochondrial disease had 501 citations, while ooplasm transfer in human cells had 58 citations. There is remarkably sparse empirical knowledge in animal studies and almost no human clinical studies on the safety and efficacy of ooplasmic transfer. There are no follow-up studies on the 30 children born through ooplasmic transfer. As one researcher wrote: “Transfer of ooplasm was thus applied with astonishing speed in humans in the absence of extensive research to evaluate the efficacy and the possible risks of the method.” That was written in 2004, and things haven’t changed.4

The few published animal studies report a clear and present danger:

• Heteroplasmy created by the mixture of cytoplasm from different strains of mice resulted in physiological impairment, including disproportionate weight gain and cardiovascular system changes.5
• Cytoplasmic transfer used in cattle produces heteroplasmic offspring.6
• Some children born through cytoplasmic transfer have been identified as heteroplasmic.7
• There is cross talk between mitochondrial DNA and nuclear DNA; it is not known but suspected that nuclear DNA cross talk between two mitochondrial genomes will affect the development of the offspring.8
• The paternal genome may be especially susceptible to epigenetic alternations by foreign ooplasm.9
• Mixing of two different mouse mitochondrial DNA within the same female germline can lead to offspring with neuro-psychiatric
defects.10

- While offering the prospect of treatment to some infertile couples, cytoplasmic transfer is “capable of generating unexpected abnormalities.”11

The authors of the most current and comprehensive review article of mitochondrial DNA and heteroplasmy, referring to ooplasmic transfer and other ART procedures, wrote that “all appropriate preclinical tests must be performed in an effort to reduce the risk for adverse outcomes”12

Many questions need to be answered before ooplasmic transfer could be considered safe and effective to the offspring. Until these questions are answered first by systematic animal studies,13 I can find no consensus within the scientific community to proceed.

Other methods for addressing the transfer of mitochondrial disease to offspring, such as Pronuclear Transfer or Maternal Spindle Transfer, introduce similar problems of heteroplasmy which have not been resolved. As noted by Spikings et al. (2006): “Other techniques, such as germinal vesicle transfer and pronuclear transfer, have been proposed as methods of preventing transmission of mitochondrial diseases to future generations. However, resulting embryos and offspring may contain mtDNA heteroplasmy, which itself could result in mitochondrial disease. It is therefore essential that uniparental transmission of mtDNA is ensured before these techniques are used therapeutically.”14

There are ethical questions concerning germ line gene modification for ooplasm transfer, Pronuclear Transfer and Maternal Spindle Transfer, which hold equal if not greater weight than the scientific questions. These issues should be addressed by a national ethics commission, which should assess whether the “three-parent genome” is a stepping stone to a new eugenics.15

Sheldon Krimsky, PhD, is Chair of the Board of Directors of the Council for Responsible Genetics, and the Lenore Stern Professor of Humanities and Social Sciences in the Department of Urban and Environmental Policy and Planning and adjunct professor in the Department of Public Health and Community Medicine at Tufts University.

Endnotes

David King, p. 19

Sheldon Krimsky, p. 22
8. Ibid.