Mitochondrial gene disorders are conditions caused specifically by mutations in mitochondrial DNA (mtDNA) and cytoplasmic DNA in the organelles that contribute to energy production and cellular respiration. These mutations can take place in somatic cells during embryonic development or during growth of the child following birth or can be inherited from the mother. The maternal transfer of these potential disease-causing mutations can be seen in one of every two-hundred newborns. The symptoms of these disorders vary between cases but typically, vital organs that depend on oxidative phosphorylation for the output of energy are most severely impacted (1).

Scientific advancement has allowed for the possibility of preventing the maternal transmission of mitochondrial gene disorders. The approach comprises of the mitochondrial DNA being replaced by a donor's healthy mitochondria. This mitochondrial gene transfer would cause the child to have the donor's mitochondrial DNA, rather than that of the mother. There are two different procedures that allow for the transfer to occur; they are called spindle transfer and pronuclear transfer. Spindle transfer is done by separating and transplanting the mother's meiotic spindle, which is formed by the chromosomes in metaphase of the oocyte (unfertilized egg) and contains nuclear DNA, into a donated vacant unfertilized oocyte. After the transfer, the reconstituted oocyte is ready to be fertilized and transplanted into the mother. Pronuclear transfer is done during the zygote stage of embryonic development, which is when the egg has already been fertilized but remains a single cell and the pronuclei are apparent. Both, the mother and donor's oocytes are fertilized. The donor's pronuclei are discarded and the mother's pronuclei are transferred into the donor's vacant zygote. The reconstituted zygote is then transplanted into the mother (1).

The ethicality of these procedures is largely questioned. The main concerns are the safety and efficacy of the procedures. Since mitochondrial gene transfer permanently changes the mitochondrial DNA, it would be permanent in the lineage. Many people believe that the human germline should not be altered. Other ethical issues concern the fact that genetic and biological material is discarded, including oocyte cytoplasts and karyoplasts with pronuclei, the child would biologically have three parents, and the long-term effects of the procedure are potentially very detrimental and not very well known (1).

Mitochondrial gene transfer for the prevention of mitochondrial gene disorders in offspring has demonstrated to be a very promising approach, despite the ethical concerns. In animal-based studies, the efficacy of this procedure was revealed to be high. The likelihood of mitochondrial gene transfer failing to prevent mitochondrial gene disorders has been tested and only demonstrated that less than 2% of the mutated mitochondrial DNA in the offspring had carried over from the mother. This is a positive finding, since the threshold for disease transmission to offspring is 60% of transferred mutated mitochondrial DNA (1). Debates over abnormalities occurring in offspring from the lack of compatibility between the different nuclear and mitochondrial DNA have also been weakened. A long-standing research project did not find any abnormalities in rhesus macaque spindle transfer offspring after merging nuclear and mitochondrial DNA of distant haplotypes. The Human Fertilization and Embryology Authority of England has conveyed that there is no current evidence suggesting that mitochondrial gene transfer is an unsafe procedure (1). The approval from this panel is very optimistic, as it allows families to undergo the much-needed procedures to prevent the transmission of mitochondrial disease. Although more research of the effects and outcomes of mitochondrial gene transfer should continue to be studied, it has demonstrated to be a very beneficial procedure.

References

1. Mitalipov, S., & Wolf, D. P. (2014). *Clinical and Ethical Implications of Mitochondrial Gene Transfer*. ms, Beaverton. Retrieved from https://scispace.com/pdf/clinical-and-ethical-implications-of-mitochondrial-gene-319etcyux5.pdf.