ESHRE 2021 Virtual (26 June – 1 July 2021)

Questions for the speakers

PCC04: How safe is Medically Assisted Reproduction and how far should we go to produce children?

Are mito-nuclear interactions likely to be problem for mitochondrial replacement therapy? - Ewa Bartnik (Poland)

Q: What is your personal view on whether the unknowns of MRT warrant selection of only male offspring at this point?

A: I do not think this is necessary, also I do not like the idea.

Q: Why are there no publications on the babies born?

A: There are two by Zhang, in one the baby was the famous one born in Mexico, in the other one the pregnancy with two embryos did not get to term. The other replacements are done – as in the second Zhang paper – to aid problems with infertility and not for mitochondrial diseases. I do not know why the Newcastle group – they have a permit for a number MRT pregnancies per year – since 2016 – have not done and/or published anything.

> John Zhang et al., *First Live Birth Using Human Oocytes Reconstituted by Spindle Nuclear Transfer for Mitochondrial DNA Mutation Causing Leigh Syndrome*, 106 FERTIL. STERIL. e375–e376 (2016);
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> **Zhang J**, Zhuang G, Zeng Y, Grifo J, Acosta C, Shu Y, Liu H. Pregnancy derived from human zygote pronuclear transfer in a patient who had arrested embryos after IVF.
> Reprod Biomed Online. 2016 Oct;33(4):529-533. doi: 10.1016/j.rbmo.2016.07.008. Epub 2016 Aug 1.PMID: 27523926

Q: Great Talk Dr Bartnik. How to transfer these concepts to patients? Public opinion and politics use this theme as if the technique was available in everyday life

A: This is a problem with many things, I am currently reviewing a high school textbook and they talk of stem cell-derived organs for transplantation. Not that there are any, so public opinion is unfortunately sometimes not aware of what is actually possible.

At least there is the one boy we know of whose parents had him through MRT. So – the technique is available, is used for other purposes than prevention of transfer of mitochondrial diseases in children of women affected with these diseases – I really do not know how this goes from the one baby born in Mexico to the many women who are afraid of having sick children. Maybe in Newcastle sometime soon?

Q: Are we being too cautious with MRT, especially when compared to some other ARTs, e.g. uterus transplantation, which seem much more dangerous, no?

A: I think uterus transplantation is an extreme thing, and I confess I do not quite get it, at least in countries where surrogacy is allowed (I have two children, and my pregnancies were reasonably OK, but not the greatest time in my life), it is a major operation – twice. But the people who are cautious seem to be the people who have the greatest experience with the method – Professor Mary Herbert and the Newcastle group in respect to MRT. Maybe the pandemic is partly responsible.

Q: Your opinion on autologous mitochondria transfer such as granulosa cells to rescue the compromised oocytes to improve fertility.

A: I do not know – this is embryology and my feeling is that if cells are old /something is wrong with them there is no particular reason why one tissue/cell type is better than another. Moreover, mitochondria will not help if the nuclear DNA has problems, and this is the case in older women.

Q: If you were a patient with a mitochondrial disease, would you prefer PGD (with the transfer of an embryo with a low mutant load) or MRT (in a respectable lab)?

A: Very difficult question, the former is not 100% certain (but considerably increases the probability of having a healthy child) but is well established, the latter if it works practically guarantees a disease-free baby. But so far there is one such baby in the world.

The health of donor children and the reason for blocking sperm donors - Peter Braad Larsen (Denmark)

Q: The sperm bank does not 'block' anymore, you can still order the donor. In the past, the donors were not visible anymore, now they are. Why this change?

A: A donor will be permanently blocked if our Genetics team assesses that the condition might be related to the donor. If a donor is permanently blocked, his sperm can only be purchased used for sibling treatment – which means, only by women who have already conceived a child with sperm from this donor.

Q: Can a donor disqualified in one bank go to another or do banks? Do you have agreements that allow a person to be blocked in all banks?

A: A donor is only allowed to donate at one center. There are contractual agreements in place, making sure that the donor has not before and will not donate to any other center in the future.

Q: Do you provide counselling for blocked donors and if yes: how do they react to this?

A: Yes. At Cryos we perform genetic counselling for all blocked donors. This is on top of the general counselling performed for all donors.

Q: What do you think of the proposal to use couple-based exp carrier screening for ARD involving the donor, with an algorithm not showing individual results?

A: I am personally in favor of this type of “genetic matching” between recipient and donor.

This is preferable compared to expanded carrier screening. With expanded carrier screening you screen for many rare genetic recessive diseases where you end up rejecting many donors without affecting the overall risk. By rejecting the donor pool, you risk less genetic variation which is even worse.

Remember that we are all carriers of several recessive diseases. We just need to make sure that our partner is not a carrier of the same recessive diseases.

Q: Can you imagine a system that would improve feedback in terms of pregnancy and disorders in offspring? For instance clinics that order sperm are responsible?

A: I see many advantages in an improvement of feedback between recipient, clinic, and sperm bank. Luckily, the system is getting better and better all the time, but there is still room for improvement. The most important change I can imagine is if we could standardize legislation (at least within the EU), so we could avoid unnecessary fertility tourism.