Genetic affinity and the right to ‘three-parent IVF’

G. Owen Schaefer¹ · Markus K. Labude¹

Received: 3 August 2017 / Accepted: 7 September 2017 / Published online: 18 September 2017
© Springer Science+Business Media, LLC 2017

Abstract With the recent report of a live birth after use of mitochondrial replacement therapy, sometimes called ‘three-parent IVF’, the clinical application of the technique is fast becoming a reality. While the United Kingdom allows the procedure under regulatory scrutiny, it remains effectively outlawed in many other countries. We argue that such prohibitions may violate individuals’ procreative rights, grounded in individuals’ interest in genetic affinity. The interest in genetic affinity was recently endorsed by Singapore’s highest court, reflecting an emphasis on the importance of biological ties found across the globe. We apply that reasoning to make the case for a right to ‘three-parent IVF’.

Keywords Rights · Three-parent IVF · Mitochondrial replacement therapy · Regulation · Assisted human reproduction · Genetic affinity

Introduction

‘Three-parent IVF’ or ‘mitochondrial replacement therapy’ (MRT) refers to a class of techniques (including pronuclear transfer, maternal spindle transfer and polar body transfer) with the same essential feature: embryos are brought to term containing the nuclear DNA of a couple undergoing IVF, but the mitochondrial DNA (mtDNA) of a third-party donor [1–3]. The procedure is fast finding its first applications in

humans, as a live birth derived from maternal spindle transfer has been documented [4]. Additionally, some reports suggest that there has been successful use of three-parent IVF in Ukraine [5] and that efforts are now underway to commercialise the procedure in Mexico [6]. Meanwhile, there is uncertainty as to how regulators should respond to the use of three-parent IVF in humans. While the UK has taken steps towards explicit authorization of the procedure for use in clinical research [7], it remains effectively banned or heavily restricted in many parts of the world, including most of Europe, the USA, Australia, New Zealand and Singapore, among others [8, 9].

Considerations that have informed the debate

A number of considerations have been put forward against the use of three-parent IVF. Chief among these are concerns about potential harms. Bioethicist Françoise Baylis summarises these as the harm to egg donors, the harm to potential offspring and future generations, the harm to specific interest groups and the harms to society at large [10]. Further, there have been doubts about the benefits of three-parent IVF. Specifically, it has been argued that portraying the procedure as ‘life saving’ is misleading, even in the context of mothers who are at risk of bearing a child with mitochondrial disease [11]. Three-parent IVF is a way of bringing healthy individuals into existence. While this may be a good thing, the procedure should not be attributed to the value of a life-saving treatment.

Here, we wish to introduce a consideration to inform the debate; we suggest that countries that ban or heavily restrict MRT risk violating the procreative rights of their citizens. We base this strong claim on a more basic right to genetic affinity, building on a recent landmark case from Singapore’s highest

✉ G. Owen Schaefer
medgos@nus.edu.sg

¹ Centre for Biomedical Ethics, Yong Loo Lin School of Medicine, National University of Singapore, Block MD 11 #02-03, 10 Medical Drive, Singapore 117597, Singapore

court that legally recognised individuals' strong interests in genetic affinity for the first time.

Recognising the interest in genetic affinity

Arguably, a strong interest in genetic affinity is already implicit in the fact that many couples struggling to start a family spend immense resources and undergo burdensome procedures in assisted reproduction to secure a child with whom they are biologically related. But some have dismissed this as a mere preference, a product of evolutionary impulse or societal pressure that does not reflect a human need or great personal project [10, 12, 13].

Consider the case *ACB v Thomson Medical*. The case involves a couple who successfully brought to term a child via IVF in Singapore, but soon became concerned that the child's appearance did not match up with the parents' ethnicity [14]. It was later confirmed that, instead of the father's sperm, a third-party anonymous donor's sperm had accidentally been used to inseminate the mother's egg in the IVF process. The couple sued their fertility clinic, and the case wound up in front of Singapore's highest court.

Due to sound concerns about devaluing life, the Court did not want to offer an award for an unwanted birth per se. However, it recognised that a great harm had been done and instead awarded substantial compensation for a new category of loss: genetic affinity. The Court reasoned that the couple sought not just to have any child, but a child that is the product of *their* gametes, who is genetically related to both of them. This was not an incidental or fleeting desire—it went to one of their core motivations for having a child and, according to the Court, reflected a legitimate interest in genetic affinity with one's children.

It should be noted that in *ACB v Thomson Medical*, there was a racial component as well. Part of the plaintiff's complaint concerned the stigma and misunderstandings the couple faced due to having a child with a somewhat different complexion than them. However, for present purposes, we would like to set aside any purported interests in the couple having a child of similar skin colour (or other superficial traits) as them. Instead, we see the interest in genetic affinity as an interest in a particular genealogical relation, where the child is the product of the mixing of the parents' genetic material. This interest would be frustrated if Thomson Medical had mixed up the intended father's sperm with the sperm of a donor of the same race.

In any case, the Court did not go so far as to acknowledge a right to genetic affinity—indeed, for the purpose of deciding the case before it, it did not need to. But we can derive such a right once we acknowledge the important connection between rights and interests. According to a widely endorsed account, rights have the function to protect interests that are of

sufficient importance to the very individual who holds the right [15]. The interest in genetic affinity may fit this role in various ways. For some people, genetics are a key part of their conception of identity and self. Philosopher David Velleman argues that this gives children a strong interest in knowing the identity of their genetic parents [16]. But it also provides a strong converse interest of parents in having children with whom they can identify [17].

Other people may derive the importance of genetic continuity and biological lineage from their religious world views [18], or from a brute but powerful urge for biologically related children [19, 20]. For these people, the importance of genetic continuity is intricately linked to the general sources of meaning in life.

Individuals' ultimate grounds for having an interest in genetic affinity may vary. However, the key point is that such grounds exist and that these, in turn, may underpin a right to genetic affinity, understood as a species of procreative rights. Such procreative rights are importantly neutral as to the specific traits possessed by the parents; they explain part of why forced sterilisation of 'undesirables' with real or perceived genetic defects during the heyday of the eugenic movement was so deeply objectionable. Prohibiting three-parent IVF may not rise to the level of wrongness of such sterilisation, but it does have a similar impact of denying women with particular disorders the opportunity to have healthy genetically related children.

The right to three-parent IVF

The right to genetic affinity has several general implications, including the right's violation in cases like *ACB v Thomson Medical*. But it may also ground the right to three-parent IVF, which is to say, the right against blanket government bans on MRT.

To illustrate, a woman with disordered mitochondria may face a dilemma: have a child naturally, risking significant mitochondrial disease in her offspring, or adopt or secure a gamete donor, giving up on her central project of having genetic affinity with her children. MRT would resolve this dilemma by allowing such women to have healthy, genetically related children. By banning MRT, governments essentially shut off a reasonable opportunity to secure genetic affinity with her children. This leads bioethicist Robert Klitzman and colleagues to claim that to 'deny women with mitochondrial disease the same opportunity to have a genetically related child as other women would be unjust' [21]. But what does the injustice consist in? Our claim provides an answer to that: to deny women with mitochondrial disease the same opportunity to have genetically related children as other women violates their *right* to genetic affinity.

The affinity is admittedly not complete because the resulting child would have the donor's mtDNA. However, mtDNA is only a very small percentage of one's overall DNA, and nuclear DNA (which is derived from the woman undergoing IVF) is generally considered much more central to our features identity. Indeed, this is what has some to claim that the term 'three-parent IVF' is a misnomer, since the contribution of the mitochondrial donor is too trivial to merit calling that donor a parent [22, 23].

Notably, recognising the right to three-parent IVF may increase the overall population—some parents who would otherwise not bear a child might instead bring a child into the world. This in turn could put a strain on resources and the environment. However, this is true of procreative rights more generally. If this is a reason to disallow MRT, this is also a reason to disallow IVF more generally and moreover a reason for restricting procreation in the general population (as what China had done with its one-child policy). But disallowing MRT while allowing other forms of procreation is as a matter of justice unfair to women with mitochondrial disorders, by selectively barring them from bearing healthy genetically related offspring.

At the same time, we should be careful that recognising the right to three-parent IVF does not impinge on the other procreative rights of women with mitochondrial disorders. Just as women with mitochondrial disorders should not be barred from accessing MRT, their procreative rights demand that they should not be barred from having children naturally. Natural childbearing may lead to the creation of individuals with very poor life prospects, but a prohibition on such conception would unduly infringe on their reproductive freedoms.

The right to three-parent IVF as a negative right

A key objection to this line of reasoning is that emphasising the importance of genetic affinity devalues non-genetic parental relations, such as adoption or IVF using donated gametes or embryos [13, 24]. However, this objection mistakes the nature of procreative rights like the right to genetic affinity. These are essentially negative rights—rights against interference in procreation by third parties, including the government. Negative rights hardly imply that individuals who do not exercise a right are deficient or making some mistake. By way of comparison, recognising and respecting the right of competent adults to refuse medical treatment hardly impugns or devalues the medical treatment itself. Instead, it recognises the interests of individuals in deciding for themselves what happens to their bodies. The same sort of recognition could extend to genetic affinity.

Conceiving of the right to MRT as a negative right also avoids another objection that has been put forward against the procedure. The objection is that research into the clinical

application of MRT 'does not meet a plausible social value standard to render public research investment into its development ethical' because the procedure's primary function is to fulfil a preference (for genetic relatedness) and not a medical need [24]. However, recognition of the negative right to 'three-parent IVF' would first and foremost speak against blanket bans or heavy restrictions on the procedure.

We leave open whether the interest in genetic affinity may reasonably be extended to ground a positive right as well, which could justify allocating public funds to MRT research. Notably, recognising such a positive right would help address potential inequalities where only well-off women with mitochondrial disorders would be able to secure genetic affinity with their children. But the demandingness of positive rights makes them more difficult to justify, and in any case, legal restrictions are currently a greater barrier to access to MRT than financial means.

Robust regulations, not blanket bans

To be clear, the right to three-parent IVF does not mean the right to *unregulated* MRT. Safety and efficacy concerns surrounding MRT must continue to guide the regulation of the procedure, especially during the experimental stage [25]. Regulations like those delineated by the Human Fertilisation and Embryology Authority (HFEA) in the UK are justified insofar as they protect the rights and interests of all individuals involved in MRT. Properly regulated systems may raise the costs of MRT, but merely raising costs of a practice does not violate rights to access. Indeed, concerns have been raised surrounding the relatively unregulated MRT procedure undertaken in Mexico, where for example, the mitochondrial donor had only signed a generic consent form for egg donation and was not told her genetic material would be used in this controversial procedure [26]; by contrast, under HFEA regulations, donor consent for MRT is required [27].

This is not to say the UK's approach is perfect. It currently only allows MRT to avoid passing on mitochondrial disorders. This leaves women with compromised fertility that could benefit from MRT in the lurch for now. But it goes further than any other country's regime in balancing the procreative rights of its population against the legitimate safety and efficacy concerns. Indeed, because MRT is part of the publicly funded healthcare system in the UK, it in a sense goes further and instantiates a positive right to subsidised IVF.

Conclusion

As the UK's experience with regulated MRT evolves, the debate about the appropriate regulatory response to the use of MRT in humans will no doubt continue. While concerns about

the risks and the safety of the procedure must be taken into account, regulators should duly balance these concerns against their citizens' presumptive rights to access three-parent IVF.

Acknowledgements We would like to thank the following individuals for their helpful input: Isabel Faber; Sharon Kaur; Lee Tsung-Ling; Voo Teck Chuan; Tamra Lysaght; Ainsley Newson; Peter Braude; the two anonymous reviewers for the Journal of Assisted Reproduction and Genetics; and attendees at the 2017 Bioethics Public Forum on Mitochondria Replacement at the Science Centre Singapore.

Funding This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Wolf DP, Mitalipov N, Mitalipov S. Mitochondrial replacement therapy in reproductive medicine. *Trends Mol Med*. 2015;21(2):68–76.
2. Falk MJ, Decherney A, Kahn JP. Mitochondrial replacement techniques—implications for the clinical community. *N Engl J Med*. 2016;374(12):1103–6.
3. Amato P, Tachibana M, Sparman M, Mitalipov S. Three-parent in vitro fertilization: gene replacement for the prevention of inherited mitochondrial diseases. *Fertil Steril*. 2014;101(1):31–5.
4. Zhang J, Liu H, Luo S, Lu Z, Chávez-Badiola A, Liu Z, et al. Live birth derived from oocyte spindle transfer to prevent mitochondrial disease. *Reprod BioMed Online*. 2017;34(4):361–8.
5. Coughlan A. First baby born using 3-parent technique to treat infertility. *New Scientist* [Internet]. 2017. Available from: <https://www.newscientist.com/article/2118334-first-baby-born-using-3-parent-technique-to-treat-infertility/>.
6. Mullin E. The fertility doctor trying to commercialize three-parent babies. *MIT Technology Review* [Internet]. 2017. Available from: <https://www.technologyreview.com/s/608033/the-fertility-doctor-trying-to-commercialize-three-parent-babies/>.
7. Sample I. First UK licence to create three-person baby granted by fertility regulator. *The Guardian* [Internet]. 2017. Available from: <https://www.theguardian.com/science/2017/mar/16/first-licence-to-create-three-person-baby-granted-by-uk-fertility-regulator>.
8. Araki M, Ishii T. International regulatory landscape and integration of corrective genome editing into in vitro fertilization. *Reprod Biol Endocrinol*. 2014;12(1):108.
9. Adashi EY, Cohen IG. Mitochondrial replacement therapy: unmade in the USA. *JAMA*. 2017;317(6):574.
10. Baylis F. The ethics of creating children with three genetic parents. *Reprod BioMed Online*. 2013;26(6):531–4.
11. Rulli T. The mitochondrial replacement “therapy” myth. *Bioethics*. 2017;31(5):368–74.
12. Baylis F. Human nuclear genome transfer (so-called mitochondrial replacement): clearing the underbrush. *Bioethics*. 2017;31(1):7–19.
13. Rulli T. Preferring a genetically-related child. *J Moral Philos*. 2016;13(6):669–98.
14. ACB v Thomson Medical Pte Ltd and others. Singapore Law Report. 2017;1:918–1014.
15. Raz J. On the nature of rights. *Mind*. 1984;XCIII(370):194–214.
16. Velleman JD. II. The gift of life. *Philos Public Aff*. 2008;36(3):245–66.
17. Kolodny N. Which relationships justify partiality? The case of parents and children. *Philos Public Aff*. 2010;38(1):37–75.
18. Bin Ibrahim AH, Abdul Rahman NN, Saifuddeen SM. Advances in tri-parent baby technology: the bioethical challenge for Muslims. In: Kamali MH, Bakar O, Batchelor DA-F, Hashim R, editors. *Islamic perspectives on science and technology: selected conference papers*. Singapore: Springer Singapore Imprint: Springer; 2016.
19. Widdows H. The impact of new reproductive technologies on concepts of genetic relatedness and non-relatedness. In: Widdows H, Idiakez IA, Cirion AE, editors. *Women's Reproductive rights*. New York: Palgrave Macmillan; 2006.
20. Edwards RG, Sharpe DJ. Social values and research in human embryology. *Nature*. 1971;231(5298):87–91.
21. Klitzman R, Toynbee M, Sauer MV. Controversies concerning mitochondrial replacement therapy. *Fertil Steril*. 2015;103(2):344–6.
22. Nuffield Council on Bioethics. Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review. London: Nuffield Council on Bioethics; 2012.
23. Dimond R. Social and ethical issues in mitochondrial donation Fig. 1. *Br Med Bull*. 2015;115(1):173–82.
24. Rulli T. What is the value of three-parent IVF? *Hast Cent Rep*. 2016;46(4):38–47.
25. Greenfield A, Braude P, Flinter F, Lovell-Badge R, Ogilvie C, Perry T. Scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception 2016 update. London: Human Fertilisation and Embryology Authority; 2016.
26. Alikani M, Fauser BCJ, García-Valesco JA, Simpson JL, Johnson MH. First birth following spindle transfer for mitochondrial replacement therapy: hope and trepidation. *Reprod BioMed Online*. 2017;34(4):333–6.
27. Human Fertilisation and Embryology Authority. Code of Practice: 8th Edition [Internet]. London; 2016. Available from: http://www.hfea.gov.uk/docs/CoP_2016_Final.pdf.