Stem cell derived gametes and uterus transplants: hurray for the end of third party reproduction! Or not?

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Introduction

Although third party reproduction has become increasingly accepted, it remains a last resort and a suboptimal option for most people, which is often only taken into consideration when reproduction with one's own gametes or own womb has proven to be impossible[1]. The paradigmatic cases for people who cannot become genetic or gestational parents/mothers are people who lack (functional) gametes and women who lack a uterus, either from birth or due to disease. In an effort to make genetic and gestational parenthood possible even for these two groups, research is being conducted aimed at deriving gametes from stem cells matched to the patient and clinical trials are ongoing for uterus transplantation. Both are examples of what Donna Dickenson has called 'Me Medicine', medical interventions focusing on individual interests, rather than on the common good[2]. However, are these also worrisome examples of Me Medicine? And is an alternative, We Medicine approach possible?

The science

Stem cell derived gametes

In order to produce gametes in vitro containing the genetic material of the patient, several steps are needed, which are all technically difficult and at present experimental. First, a stem cell line needs to be created matching the patient's genome. This can currently be done in two ways. The first technique – called somatic cell nuclear transfer (SCNT) or 'therapeutic cloning' – involves the transfer of the cell nucleus of a somatic cell of the patient (for example a skin cell) into an enucleated egg cell. The egg cell will then erase the epigenetic marks on the nuclear DNA and on activation an embryo can be grown which is genetically identical to the patient (not taking the mitochondrial DNA into consideration). When this embryo reaches the blastocyst stage (after 5 days), the inner cell mass can be extracted and cultured, resulting in an embryonic stem cell line. The second technique is direct reprogramming, resulting in induced pluripotent stem cells (iPS cells). In this scenario, somatic cells are reverted to their embryonic state by adding a small number of specific factors, a technique for which the Nobel prize in physiology or medicine was awarded to Sir John B. Gurdon and Shinya Yamanaka in 2012. Once a stem cell line has been established containing the DNA of the patient, gametes (ideally sperm or egg cells, or precursors of those cells) need to be derived from those stem cells. In the mouse model, significant progress has been made in the last decade, resulting in the

[1] Elia Wyverkens, Veerle Provoost, An Ravelingien et al, 'The meaning of the sperm donor for heterosexual couples: confirming the position of the father' (2015) 56 *Family Process* 203-216.

[2] Donna Dickenson, Me Medicine vs. We Medicine: Reclaiming Biotechnology for the Common Good. (New York: Columbia University Press, 2013).

creation of functional sperm cells *in vitro*, which produced live offspring in 2016[3] [4] [5] [6] [7] [8]. Before transferring this science to clinical trials in humans, much research remains to be done regarding the safety of the procedure. Given the profound manipulations, the residual risks for the children who are conceived with these stem cell derived gametes due to genetic, epigenetic, transcriptomic and imprinting problems is likely to remain higher than for the established option of donor conception, even after preclinical animal and embryo research. Moreover, follow-up over several generations will be necessary in order to confirm that the technology is really safe.

Uterus transplantation

Unlike stem cell derived gametes, uterus transplantation is already in the phase of clinical trials. After unsuccessful clinical trials in Saudi-Arabia and Turkey, several children have been born thanks to uterus transplantation in a Swedish clinical trial involving 9 patients and recently the first birth in the US was reported in the media[9] [10] [11]. A uterus transplantation involves an extensive surgical procedure for both the donor and the recipient. Donor surgery typically lasts between 10 and 13 hours and recipient surgery between 4 and 6 hours (there does not seem to be a learning curve yet)[12]. One reported donor complication is ureterovaginal fistula (1 case). Postoperative recipient complications include thrombosis or infections, which led to the removal of the transplanted uterus in two cases, pleural fluid (which was spontaneously resorbed) and a haematoma (requiring blood transfusion).

After the transplantation, the recipient needs to take immunosuppressive drugs in order to avoid rejection. Johansson *et al*. report rejection episodes in five of seven recipients (some had multiple rejection episodes)[13]. All but one were classified as mild and all rejection episodes were without clinical symptoms. Immunosuppression implies that patients are more susceptible to, for example,

[3] Karin Hübner, Guy Fuhrmann, Lane K. Christenson *et al*, 'Derivation of oocytes from mouse embryonic stem cells' (2003) 300 *Science* 1251-1256.
[4] Yayoi Toyooka, Naoki Tsunekawa, Ryuko Akasu and Toshiaki Noce T, 'Embryonic stem cells can form germ cells in vitro' (2003) 100 *Proceedings of the National Academies of Sciences of the United States of America* 11457–11462.
[5] Niels Geijsen, Melissa Horoschak, Kitai Kim, Joost Gribnau, Kevin Eggan and George Q. Daley, 'Derivation of embryonic germ cells and male gametes from embryonic stem cells' (2004) 427 *Nature* 148-154.
[6] Karim Nayernia, Jessica Nolte, Hans W. Michelmann, *et al*, 'In vitro-differentiated embryonic stem cells give rise to male gametes that can generate offspring mice' (2006) 11 *Developmental Cell* 125-132.
[7] Katsuhiko Hayashi, Sugako Ogushi, Kazuki Kurimoto *et al*, 'Offspring from oocytes derived from in vitro primordial germ cell–like cells in mice' (2012) 338 Science 971-975.
[8] Quan Zhou, Mei Wang, Yan Yuan *et al*, 'Complete meiosis from embryonic stem cell-derived germ cells in vitro' (2016) 18 *Cell Stem Cell* 330-340.
[9] Mats Brännström, Liza Johannesson, Hans Bokström *et al*, 'Livebirth after uterus transplantation' (2015) 385 *The Lancet* 607-616.
[10] Mats Brännström, Hans Bokström, Pernilla Dahm--Kähler *et al*, 'One uterus bridging three generations: first live birth after mother-to-daughter uterus transplantation' (2016) 106 *Fertility and Sterility* 261-266.
[11] Alexandra Sifferlin, 'Exclusive: First U.S. Baby Born After a Uterus Transplant' (2017) *Time*, Published December 1, 2017. Available at http://time.com/5044565/exclusive-first-u-s-baby-born-after-a-uterus-transplant/
[12] Mats Brännström, Liza Johannesson, Pernilla Dahm-Kähler, *et al*, 'First clinical uterus transplantation trial: a six-month report' (2014) 101 *Fertility and Sterility* 1228-1236.
[13] Liza Johannesson, Niclas Kvarnström, Johan Mölne *et al*, 'Uterus transplantation trial: 1-year outcome' (2015) 103 *Fertility and Sterility* 199-204.

viral infections and certain cancers. For the foetus, several immunosuppressive regimens are considered to be safe[14], although caution and follow-up is warranted as there is still a great deal of conflicting evidence[15].

All officially reported deliveries were preterm caesarean sections. In the first case reported, the mother developed pre-eclampsia in the 32nd week of pregnancy; in the second case, the delivery was preterm due to cholestasis[16] [17]. The weight of the children was low due to the preterm birth, but – fortunately – well within the average weight for their gestational age.

A category of patients with absolute uterine factor infertility who might benefit from uterus transplantation are patients with Mayer-Rokitansky-Küster-Hauer (MRKH) syndrome, with congenital absence of uterus and vagina. This syndrome is also oftentimes accompanied by renal problems such as kidney malformation, single kidneys or pelvic kidneys, which can cause additional risks during pregnancy and delivery, for example pre-eclampsia. Eight out of the nine patients in the Swedish clinical trial are MRKH-patients[18].

In short, we can say that although there is proof of principle that it is possible to deliver a healthy baby after a uterus transplantation, these are high-risk pregnancies which require invasive surgical procedures for the patient and the healthy research participant (the uterus donor). In other words, it is *not* a proof of principle that uterus transplantation is safe. Attempts have been made to use a uterus from a deceased donor (in order to avoid harming at least one of the participants in these experiments), which has both advantages and disadvantages from a technical perspective. At the time of writing, there have been a number of successful transplants from deceased donors, but no live births have been reported[19] [20].

Why do we transplant uteri? Why do we attempt to make eggs and sperm in vitro?

Uterus transplantation and in vitro gametogenesis are not among the usual examples of personalised or 'Me' medicine, which is often identified with genomic medicine (see the introduction to this volume). Yet they certainly fit within the broader paradigm: they are very individualistic solutions for very personal desires. Also, as will be argued below, although research in these areas may further the interests of individual patients, the balance in terms of overall healthcare benefit may turn out to be negative, rather than positive. It is therefore unsurprising that the four possible drivers of

[14] Lisa A. Coscia, Serban Constantinescu, John M Davison *et al*, 'Immunosuppressive drugs and fetal outcome' (2014) 28 *Best Practice & Research Clinical Obstetrics & Gynaecology* 1174-1187.
[15] Giuseppe Benagiano, Laurens Landeweerd and Ivo Brosens, 'Medical and ethical considerations in uterus transplantation' (2013) 123 *International Journal of Gynecology & Obstetrics* 173-177.
[16] Mats Brännström, Liza Johannesson, Hans Bokström *et al*, 'Livebirth after uterus transplantation' (2015) 385 *The Lancet* 607-616.
[17] Mats Brännström, Hans Bokström, Pernilla Dahm--Kähler *et al*, 'One uterus bridging three generations: first live birth after mother-to-daughter uterus transplantation' (2016) 106 *Fertility and Sterility* 261-266.
[18] Mats Brännström, Liza Johannesson, Pernilla Dahm-Kähler *et al*, 'First clinical uterus transplantation trial: a six-month report' (2014) 101 *Fertility and Sterility* 1228-1236.
[19] Omer Ozkan, Munire Erman Akar, Ozlenen Ozkan *et al*, 'Preliminary results of the first human uterus transplantation from a multiorgan donor' (2013) 99 *Fertility and Sterility* 470-476.
[20] Giuliano Testa, Tiffany Anthony, Gregory J. McKenna *et al*, 'Deceased donor uterus retrieval: A novel technique and workflow' (2017) *American Journal of Transplantation* DOI: 10.1111/ajt.14476

personalised medicine (at the expense of We Medicine) as discerned by Donna Dickenson can also be applied to the contexts of gamete derivation and uterus transplantation: (1) threat and contamination, (2) narcissism and "bowling alone", (3) corporate interests and political neoliberalism, and (4) the sacredness of personal choice.

First, threat and the fear of contamination can be linked to fear of third party involvement in the formation of a family. In the case of adoption, parents may wonder if the child has been psychologically damaged by being abandoned by its parents. In the case of surrogacy, parents may he worried about the impact of the behaviour of the women carrying their child (Does she drink alcohol? Does she eat healthily? Does she take folic acid?) and about the possibility that there may be an emotional bond between her and their child. In the case of donor conception, parents may worry about the donor being perceived as the 'real parent' or about 'flaws' in their children due to the donor's contribution.

Second, narcissism and bowling alone is reflected in the importance that is attached to genetic parenthood. This is not only important in the context of stem cell derived gametes, but also plays a role in the enthusiasm surrounding uterus transplantation, as surrogacy (which is the only alternative option if a genetic link is to be established) is not an available alternative in many countries. As mentioned, in Sweden, where the successful clinical trial for uterus transplantation is taking place, surrogacy is prohibited. In *Me Medicine versus We Medicine: Reclaiming Biotechnology for the Common Good*, Dickenson links narcissism with the 'genetic mystique' (giving DNA a soul-like status) and genetic determinism (believing that we are determined by our genes)[21]. These phenomena may indeed do much of the explanatory work of why people think it is so important to pass on their genes to their children and why they want to avoid genes from strangers to enter 'their' gene pool.

Third, corporate interests might reinforce the technological imperative of moving these new technologies to the clinic as fast as possible. Offering the newest technology to patients can be perceived by the latter as a sign of excellence, of being a state-of-the-art clinic. We will, however, not discuss this element any further.

Finally, the sacredness of personal choice is very prominent in this debate. Under the flag of reproductive liberty or reproductive autonomy, it is insinuated that everyone has the right to have genetically related children and that every woman has the right to gestate her own children (if at all possible). If one accepts this premise (which sounds deceptively self-evident to many) and if one takes as a given that for some people, the only option of granting this right is by uterus transplantation or gamete derivation, then it logically follows that people have the right to have access to uterus transplantation and stem cell derived gametes.

These three reasons why uterus transplantation and SCD gametes are so welcomed – the avoidance of third party involvement, the importance of genetic and gestational parenthood and the emphasis on reproductive rights – will be further elaborated on below.

Threat and contamination: "Third party reproduction is problematic"

[21] Donna Dickenson, Me Medicine vs. We Medicine: Reclaiming Biotechnology for the Common Good. (New York: Columbia University Press, 2013), p 15.

There are different ways of making this argument, some more convincing than others.

First, some people question the morality of any kind of third party reproduction in favour of the traditional family unit (one father and one mother). This can be based on a number of grounds, both religious and secular. Some religions equate sperm donation with adultery or claim that third party involvement in reproduction violates the holy union between husband and wife and the sacred act of conception. The Catholic Church and Sunni Muslims, for example, do not approve of donor conception[22] [23]. On the secular side, objections that donor conception is unnatural and concerns for the welfare of the future child are voiced, as third party reproduction would, for example, impact on their identity formation[24].

Second, for the parents, the involvement of an outsider in the creation of their family can be emotionally troubling. The romantic image of creating a new individual by joining characteristics of two partners into one and/or of carrying a partner's child to term is shattered, which may result in a sense of failure. Moreover, the donor presents a threat to the family unit and more specifically to the legitimacy of the parental role of the 'social parent', or is at least perceived as such[25]. This fear is possibly even greater in jurisdictions where donor anonymity has been lifted. Surrogacy may involve the fear that the surrogate will become emotionally attached to the child and claim a parental role. Also, it is difficult for a couple to start bonding with their child before birth and the intended parents may disagree with the surrogate about permissible lifestyle habits or more profound decisions regarding the pregnancy (such as a reduction of a multiple pregnancy, for example).

Third, the practical implications of third party reproduction have proven to be an ethical minefield. Concerns for exploitation and commodification are linked to oocyte donation and surrogacy, there is fierce ongoing debate worldwide about the acceptability of donor anonymity, there have been sporadic reports of custodial battles, abandoned and stateless children and of embryo trading, there are concerns about sperm donors transmitting genetic diseases, et cetera[26] [27] [28] [29] [30] [31] [32] [33].

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[22] Marcia C. Inhorn, 'Making Muslim babies: IVF and gamete donation in Sunni versus Shi'a Islam' (2006) 30 *Culture, medicine and psychiatry* 427-450.

[23] Julie H. Rubio, 'Family ties: A Catholic response to donor-conceived families' (2015) 21 *Christian Bioethics* 181-198.

[24] Amanda J. Turner and Adrian Coyle, 'What does it mean to be a donor offspring? The identity experiences of adults conceived by donor insemination and the implications for counselling and therapy' (2000) 15 *Human Reproduction* 2041-2051.

[25] Elia Wyverkens, Veerle Provoost, An Ravelingien *et al*, 'The meaning of the sperm donor for heterosexual couples: confirming the position of the father' (2015) 56 *Family Process* 203-216.

[26] Nicole Bromfield and Karen Smith Robati, 'Global Surrogacy, Exploitation, Human Rights and International Private Law: A Pragmatic Stance and Policy Recommendations' (2014) 1 *Global Social Welfare* 123-135.

[27] I. Glenn Cohen, 'Sperm and Egg Donor Anonymity'. In Leslie Francis (Ed.), *The Oxford Handbook of Reproductive Ethics* (Oxford: Oxford University Press, 2016).

[28] Donna Dickenson, *Property in the Body: Feminist Perspectives* (Cambridge: Cambridge University Press, 2017, 2nd ed.), pp 65-87.

[29] Anders Hansen, 'Danish sperm donor passed neurofibromatosis on to five children' (2012) 345 *British Medical Journal (Online)* e6570.

[30] Mark Henaghan, 'International surrogacy trends: How family law is coping' (2013) 7 *Australian Journal of Adoption*. Retrieved from http://www.nla.gov.au/openpublish/index.php/aja/article/view/3188.

[31] Barry J. Maron, John R. Lesser, Nelson B. Schiller *et al*, 'Implications of hypertrophic cardiomyopathy transmitted by sperm donation' (2009) 302 *Journal of the American Medical Association* 1681-1684.

Against this backdrop, it is unsurprising that many research efforts are aimed at methods to avoid third party involvement in reproduction. However, while uterus transplantation and in vitro gametogenesis avoid some of the objections to surrogacy and donor conception mentioned above, it does not logically follow that they are more acceptable and less problematic, as they present their own ethical concerns, primarily in terms of safety, as mentioned above. Also, even if – under certain circumstances – they would be the better option to achieve the goal of parenthood as compared to third party reproduction (or in some jurisdictions the only legal option), that does not automatically legitimize them, as will be discussed below.

Narcissism and 'bowling alone': "Genetics/gestation is very important"

Both genetics and gestation tend to be portrayed in terms of basic human needs, rather than in terms of personal desires. This portrayal makes it easier to argue for investments in reproductive medicine in general and paves the way for greater acceptance of costly high-tech innovations in this domain, as has been remarked by Françoise Baylis and Alana Cattapan in the context of human nuclear genome transfer[34] [35].

A first way of addressing the claim that genetics and gestation are very important in family relationships is to refer to family functioning. However, family functioning in families created through third party reproduction has been reported to be well within the normal range[36] [37]. Moreover, even in those cases where family functioning *is* affected or where higher levels of stress and anxiety are reported, one can wonder whether this is due to the absence of the genetic/gestational link in itself or due to the narratives that accompany alternative ways of family creation. For example, it is very unlikely that the absence of a genetic link would have any effect on family functioning as long as the parents were unaware of the fact that they are not the genetic parents of the child (for example after an IVF mix-up). As previously argued, *genetic* parenthood is not the objective, biological concept that it once was or that we take it to be, as illustrated by debates over who the genetic parents of clones would be and whether mitochondrial transfer really generates 'three-parent babies'. Also, although it is unsurprising from an evolutionary perspective that we have a preference for raising genetically related children, this does not explain why we legitimise this evolutionary urge, why a genetic link to our children *should* matter[38].

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[32] Usha R. Smerdon, 'Crossing bodies, crossing borders: International surrogacy between the United States and India' (2008) 39 *Cumb. L. Rev* 15-85.
[33] Stephen Wilkinson, 'The exploitation argument against commercial surrogacy' (2003) 17 *Bioethics* 169-187.
[34] Françoise Baylis, 'Human Nuclear Genome Transfer (So-Called Mitochondrial Replacement): Clearing the Underbrush' (2017) 31 *Bioethics* 7–19.
[35] Françoise Baylis and Alana Cattapan. 'Personalized Medicine and the Politics of Human Nuclear Genome Transfer', in B. Van Beers, S. Sterckx and D. Dickenson (eds.), Personalised Medicine, Individual Choice and the Common Good (Cambridge University Press, 2018), pp. XX-XX.
[36] Susan Golombok, Jennifer Readings, Lucy Blake, Polly Casey, Alex Marks and Vasanti Jadva, 'Families created through surrogacy: Mother–child relationships and children's psychological adjustment at age 7' (2011) 47 *Developmental psychology* 1579-1588.
[37] Lucy Blake, Vasanti Jadva and Susan Golombok, 'Parent psychological adjustment, donor conception and disclosure: a follow-up over 10 years' (2014) 29 *Human Reproduction* 2487-2496.
[38] Heidi Mertes, 'Gamete derivation from stem cells: revisiting the concept of genetic parenthood' (2014) 40 *Journal of medical ethics* 744-747.

Note that the latter question only becomes relevant when other issues are in the balance, for instance safety for the resulting children. If I have an irrational, evolutionary urge to have genetically related children and I harm no-one in the process of pursuing that urge, there is not a problem. This changes when I request a medical treatment that puts other individuals in harm's way (i.e. a uterus donor) or that has a higher chance of resulting in the birth of a child with a disability than available alternatives (i.e. conception with SCD-gametes as opposed to donor gametes). In these cases I will need to back up my desire with good reasons, justifying why the (moral) benefits of gratifying my desire for a genetic child outweigh the (moral) disadvantages. While acknowledging that the absence of genetic parenthood – when desired – *can* lead to a decrease in subjective wellbeing and to a sense of loss of purpose in life, and that this suffering can justify public funding of medical interventions such as IVF, it does not necessarily justify the risks involved in reproduction with SCD-gametes or in uterus transplantation.

Concerning the importance of *gestational* parenthood, a first observation is that essentialist discourse about what it means to be a mother tends to incorporate pregnancy. However, this is but one possible discourse, which is challenged by adoption and 'queer motherhood'[39]. Moreover, a simple but strong counterargument against the belief that pregnancy is of such great importance that it would justify the introduction of uterus transplantation into the clinic is that the male half of the world's population is not capable of bearing children and yet, this is not problematised at all. We do not regard the father as being less of a parent because he does not gestate children, so consistency demands that a mother who does not gestate her children is not regarded as less of a parent either. One might reply that gestation is not a crucial facet of *parent*hood, but that it is a crucial facet of *mother*hood. Indeed, it is right that not gestating deprives a woman of a facet that is typical of motherhood. However, does this deprivation carry much moral weight? And if so, why? A woman who delivers her child through a caesarean section instead of a natural birth is also deprived of a typical feature of motherhood, but one would think that the other aspects of parenthood and motherhood easily trump this missing feature. The same can be said about gestation: is the experience of pregnancy really worth risking prematurity, pre-eclampsia, or thrombosis? Moreover, on a more practical note, the experience of a pregnancy with a transplanted womb as compared to one's own womb differs significantly as the nerves are not connected and therefore the pregnant woman will not feel much of the foetal movements or contractions.

In short, it is far from obvious that the desire for genetic or gestational parenthood can trump considerations for the welfare of the future child, for the safety of the other parties involved (in the case of uterus transplantation) or that it can justify resource allocation to these new reproductive technologies.

Sacredness of personal choice: "Everyone has the right to reproduce"

The most straightforward answer to this claim is that the right to reproduce is a liberty right instead of a claim right, which therefore does not amount to a duty on society to accommodate that right.

[39] Elisabeth A. Suter, Leah M. Seurer, Stephanie Webb *et al*, 'Motherhood as Contested Ideological Terrain: Essentialist and Queer Discourses of Motherhood at Play in Female–female Co-mothers' Talk' (2015) 82 *Communication Monographs* 458-483.

This counterargument is well rehearsed in the legal and ethics literature on reproductive medicine[40] [41] [42]. Moreover, rights are always to be balanced against other people's rights, for example the right not to be harmed. Both in the case of uterus transplantation and of gamete generation, there is a trade-off between the prospective parents' desire for (genetic / gestational) parenthood on the one hand and the welfare of the donor, recipient and resulting children. In transplantation medicine, living organ donation always involves invasive surgical procedures on healthy people without a direct benefit to the donor. This appears to violate the physician's oath to 'do no harm', but in many jurisdictions, this infraction is accepted in cases where the donor provides her informed consent and when the intervention can save the life of the recipient. However, in uterus transplantation, the bar is set lower: the transplant is not aimed at the survival of the recipient or a profound increase in her quality of life.

Besides concerns for the donor's welfare, respecting reproductive autonomy does not mean that doctors should always cater to patient demand, especially in domains as emotionally charged as reproduction. Infertile women have previously been reported to be particularly vulnerable to the appeal of the technological imperative[43] [44]. For many women, it is important for their peace of mind that they 'did everything they could', regardless of the clinical, financial and emotional repercussions, almost as if they do not want to abandon a child that is waiting somewhere to be brought into existence. It is therefore all too easy for physicians to say that the procedure is legitimized by the patient's informed consent, as the validity of that informed consent can be seriously contested and as the establishment of high risk pregnancies, even with a woman's consent, can hardly be considered as good clinical practice. Several authors have referred to the danger of the therapeutic misconception, both in the minds of doctors/researchers and patients/participants, in the context of uterus transplantation clinical trials[45] [46]. Ideally, the prime motivation of participants in clinical trials should be to advance knowledge about the safety and feasibility of new medical procedures. However, in the context of uterus transplantations, this requirement is completely unrealistic. The primary motivation for women to participate in these clinical trials is their desire to gestate a baby and become a parent. There are no clinical trials set up recruiting women without a desire for motherhood, merely studying survival of the graft and it would be very unlikely that such trials would be approved by ethics committees. The therapeutic misconception is therefore not a misconception in the sense that the aim – even in the clinical trials – is primarily therapeutic. Yet, it remains important that participants are warned that while a therapeutic benefit is possible and aimed at, it is not likely and that they may end up worse off after completion of the trial than they were before.

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[40] Carter J. Dillard, 'Rethinking the procreative right' (2007) 10 Yale Human Rights and Development 1.
[41] John A. Robertson, 'Embryos, families, and procreative liberty: the legal structure of the new reproduction' (1985) 59 *Southern California Law Review* 939-1041.
[42] Laura Shanner, 'The right to procreate: when rights claims have gone wrong' (1994) 40 *McGill Law Journal* 823-874.
[43] Judith C. Daniluk, ' "If We Had It to Do Over Again...": Couples' Reflections on Their Experiences of Infertility Treatments' (2001) 9 The Family Journal 122-133.
[44] Tjeerd Tymstra, ' 'At least we tried everything': About binary thinking, anticipated decision regret, and the imperative character of medical technology' (2007) 28 *Journal of Psychosomatic Obstetrics & Gynecology* 131-131.
[45] Kavita Shah Arora and Valarie Blake, 'Uterus transplantation: the ethics of moving the womb' (2015) 125 *Obstetrics & Gynecology* 971-974.
[46] Arthur L. Caplan, Constance M. Perry, Lauren A. Plante *et al*, 'Moving the womb' (2007) 37 *Hastings Center Report* 18-20.

One can also legitimately wonder whether the welfare of the future child has received adequate consideration in the ongoing clinical trials of uterus transplantation. Despite the births of several healthy children, it might be only a matter of time before a baby gestated in a transplanted uterus suffers lifelong consequences of prematurity or other pregnancy complications linked to the transplant. Some might invoke the non-identity problem[47] to argue for a very low threshold of wellbeing in the case of stem cell derived gametes: the resulting children are not harmed as they would not have existed without this technology, unless if their lives are not worth living (the wrongful life standard). Technically speaking, this argument does not apply in the context of uterus transplantation. The future children growing from the transferred IVF-embryos have better prospects if they are carried to term by a healthy gestational carrier, than if they are carried to term in a transplanted uterus (although this interpretation was challenged by John Robertson[48]). They can therefore be said to be harmed – or at least put into harm's way – by being the subject of an experimental procedure.

Despite the non-identity problem (in the case of SCD gametes), other ethical principles give reason for a cautious approach when risks for the future children are present. First, when aspiring parents need to choose between two modes of conception, all other things being equal, it is better to choose the one that is most likely to result in healthy children (that is, they should choose those children who are most likely to suffer the least), although it is not necessarily immoral to take limited risks in regard to the future child's well-being[49]. Second, it has been argued that the most appropriate welfare standard for future children is the 'reasonable welfare standard', meaning that "[t]he provision of medical assistance in procreation is acceptable when the child born as a result of the treatment will have a reasonably happy life"[50]. Third, physicians and parents have a shared responsibility regarding the welfare of the children who are created by means of assisted reproduction. The physician therefore needs to make his or her own assessment of the harms and benefits involved for all parties. After decades of successful efforts to make pregnancy and childbirth safer for both mother and child, uterus transplantation and reproduction by stem cell derived gametes seem to be a step back, rather than a step forward.

Importantly, it is dishonest to weigh the efforts and risks for mother, child and donor against the birth of a healthy baby. The healthy live births that are reported are not the only attempts made to establish pregnancies through uterus transplantation. The hardship endured by all the couples in the clinical trial whose desire for a child was not met should therefore also be taken into account. This new innovation may provide hope to many involuntarily childless women with uterine factor infertility, but for most of them – and even many of the ones who have access to the technology – this hope will turn out to be false hope and for some of them, their adventure may end in tragedy in case of serious morbidity. This is a factor that should also be incorporated into the equation and that is easily forgotten in the excitement of a success story.

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[47] Derek Parfit, *Reasons and persons* (Oxford: Oxford University Press, 1984).

[48] John A. Robertson, 'Impact of uterus transplant on fetuses and resulting children: a response to Daar and Klipstein' (2016) 3 *Journal of Law and the Biosciences* 710.

[49] Julian Savulescu and Guy Kahane, 'The moral obligation to create children with the best chance of the best life' (2009) 23 *Bioethics* 274-290.

[50] Guido Pennings, 'Measuring the welfare of the child: in search of the appropriate evaluation principle' (1999) 14 Human Reproduction 1146-1150.

Also, on a more speculative note, the fact that there is a proof of principle that women without a uterus are able to gestate their child, but that this treatment option is beyond reach for the great majority of women, may hinder the coping process of that majority and lead to additional frustration. Therefore, if the group of patients as a whole is considered, the cost-benefit analysis may turn out to be very grim. The same reasoning would apply for patients 'needing', but not having access to SCD-gametes. In the latter context, it has been noted that by developing the technology of in vitro gametogenesis needs are being created for categories of people that currently are not labelled as infertile (such as same-sex couples or postmenopausal women), but at the same time these needs are not met[51]. Paradoxically, a focus on reproductive liberty may therefore lead to a frustration of that same liberty.

The common good and We Medicine

Moreover, as repeatedly pointed out by Dickenson[52] [53], an increased focus on individual rights in biotechnology and bioethics has diverted attention away from the common good. While this is not – and should not be – an either-or story, it is interesting to consider how we might approach the given problem (grief caused by the inability to achieve genetic/gestational parenthood) from a common good perspective. In any case, taking a broader perspective does not mean that the personal suffering caused by infertility should be minimised. It has been well established that people who are faced with a diagnosis of infertility suffer tremendously. As an indication: the same degree of depression is reported in infertility patients as in cancer patients[54]. The no-treatment option is not an option. People who suffer from infertility should receive appropriate care.

However, this does not equal giving them what they want (a baby), regardless of the risks, efforts and of whether society can afford it. If we take a step back and look at infertile people as a group, they may be very ill served by constantly confirming and thereby reinforcing the idea that one is only 'truly' a mother if one has gestated her own child and that one is only 'truly' a parent if one is a genetic parent. Many people are excellent parents to children whom they did not gestate and who did not spring from their genes. I am not only referring to third party conception here, but also to adoption, foster care, stepparents and even involved aunts and uncles. Moreover, many people lead a perfectly happy and satisfying child-free life. In terms of wellbeing, there have been numerous studies showing that there is no positive correlation between having children and happiness or life satisfaction[55]. The message that genetics and gestation are *not* necessary components of parenthood and that parenthood is *not* a necessary requirement for a meaningful life should receive adequate attention, despite the fact that patients are unreceptive to this message. Let us not forget that at

[51] Anna Smajdor and Daniela Cutas, 'Will artificial gametes end infertility?' (2015) 23 *Health Care Analysis* 134-147.
[52] Donna Dickenson, *Me Medicine vs. We Medicine: Reclaiming Biotechnology for the Common Good*. (New York: Columbia University Press, 2013).
[53] Donna Dickenson, 'The Common Good'. In Roger Brownsword, E Scotford and K. Yeung (Eds.), *The Oxford Handbook of Law, Regulation and Technology* (Oxford: Oxford University Press, 2017), p 135.
[54] Alice D. Domar, Patricia C. Zuttermeister and Richard Friedman, 'The psychological impact of infertility: a comparison with patients with other medical conditions' (1993) 14 *Journal of Psychosomatic Obstetrics and Gynaecology* 45-45.
[55] Thomas Hansen, 'Parenthood and happiness: A review of folk theories versus empirical evidence' (2012) 108 *Social Indicators Research* 29-64.

present, a large percentage of women who get on the ART-rollercoaster end up childless (for example, for US patients receiving iVF with their own gametes in 2014: 30% of patients below 35, 42% or patients between 35 and 37, 59% of patients between 38 and 40, 78% of patients between 41 and 42 and 93% of patients above 42 years are unsuccessful[56]). All these women and their partners balance several years between hope and despair and are left empty-handed. It is often only at this point of their journey – if at all – that they will get the message that life is possible without (genetically related / personally gestated) children, after years of receiving the opposite message.

Thus, if we look at the group of infertile people, are they really helped by ever new options that provide hope for all, but only a child for the happy few? Perhaps we need a new approach, whereby we content ourselves with the idea that we attempt to satisfy the desire for parenthood within certain safety limits and within certain financial constraints and that those who fall outside these limits are helped in a different way. Specifically, this would mean helping them find out what it is they are looking for in genetic parenthood or gestational parenthood and try to accommodate these desires in a different, safer, manner and/or by helping them cope with infertility.

Conclusion

Faced with the hope and hype surrounding stem cell derived gametes and uterus transplantation, we need to stop and wonder whether the goal of assisting people in their reproductive endeavours is blinding us to the 'collateral damage' that it is causing. If fertility clinics are really interested in helping *all* infertile people, the right approach is not to invest in high-tech solutions that are likely to remain elite-medicine for many years and help only a limited number of people. Rather, efforts are needed to replace Me Medicine by We Medicine when possible. One way of doing this is by critically questioning the beliefs on which the patient request is based, rather than accommodating and thereby confirming and reinforcing them. It should be brought to patients' attention that genetics and gestation are not essential elements of parenthood; that third party reproduction is not necessarily problematic or inferior; that the desire for genetic and gestational parenthood or an appeal to reproductive autonomy does not automatically justify the risks of uterus transplantation and reproduction through SCD gametes; and that parenthood is not a necessary requirement for a happy, meaningful or satisfying life. Although changing people's beliefs takes time, tackling these myths will in the long run have a bigger chance of reducing the suffering of people faced with infertility than reinforcing them.

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