



Impact of uterus transplant on fetuses and resulting children: a response to Daar and Klipstein

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In assessing the safety of uterine transplant, the effects of gestation on mother, fetus, and resulting child need close attention. Data from current and future clinical studies should provide helpful information about those concerns. Unless the risks to mother and child are acceptable, uterus transplant will not become an accepted procedure for uterine infertility.

Professor Judith Daar and Dr Sigal Klipstein in a trenchant yet generously toned comment critique my article on uterus transplant (and those of previous commentators) for a lack of focus on those risks.¹ They argue that the safety record of gestational surrogacy² in the United States is so much better than the vascular and teratogenic problems that are likely to arise with uterus transplants that women have an obligation to use surrogacy rather than transplant.³

I am very grateful for their Comment (as should be others working on uterus transplant) for they raise important questions about the effects of gestation in a donor uterus that need answering during the current experimental phase of uterus transplant.⁴ If their empirical suspicions stand, uterine transplant may not meet the high standards of safety and efficacy required to become a routine therapy.

¹ Judith Daar & Sigal Klipstein, *Refocusing the Ethical Choices in Womb Transplant, Peer Commentary Reviewing John A. Robertson, Other women's Wombs: Uterus Transplant and Gestational Surrogacy*, 3 J. L. & BIOSCI. (2016) (in press) doi:10.1093/jlb/lsw031. The article generating their comment refers to risks from immunosuppressive drugs but passes over the vascularization problems that may be even more of a concern.

² I use the term 'surrogacy' for 'gestational surrogacy' in this response.

³ They do not state such a duty explicitly, but that is the implication of their critique, at least if their data assumptions stand up. In addition, they do not address whether transplant would be acceptable if surrogacy is not available.

⁴ Dr Robert Stillman has also made this critique, though he too overlooks situations in which surrogacy is not available. See Daar & Klipstein, *supra* note 1 at 5.

The essence of their argument is that surrogacy has fewer gestation-related risks and thus is preferable to transplant, with its chance of impaired blood flow to the placenta, clotting, preeclampsia, and preterm birth and the impact of those events on mother, fetus, and resulting child. Since there is a greater risk of fetal or offspring harm with transplant, they argue that the ethical duty of procreative beneficence⁵ imposes a duty on prospective parents to choose gestational surrogacy over uterus transplant.⁶ Although I disagree with their conclusion, I commend them for highlighting a crucial issue in evaluating uterus transplant.

RESULTING CHILD NOT FETUS

To evaluate their argument, we must first be clear that their concern is with the resulting child and not the fetus *qua* fetus, as well as the mother. While they talk about ‘the developing fetus’ and ‘fetus’⁷, they also refer to ‘the child’, ‘potential child’, and ‘resulting offspring’.⁸ It seems clear that they mean fetus ‘by virtue’ of the fact that the fetus in a transplanted uterus will be born, even if it is born prematurely. If so, it is the welfare of the resulting child that is of concern and not the fetus itself. Indeed, their reliance on procreative beneficence explicitly assumes a resulting child. Of course, miscarriage after a transplant, assisted reproduction, or any pregnancy, may be a great loss to parents. But even if pregnancy is intentionally terminated, it is not a moral harm for persons who do not believe that the fetuses do not have moral status in themselves until they are born.⁹ That is, the harm they allege of uterus transplant is to a child who is born and suffers injuries or diminished capacity as a result of the transplant when surrogacy would have been equally available.¹⁰ They do not, however, address the question of whether uterus transplant may occur if surrogacy were not available.

A challenging situation would arise when signs of miscarriage, vascular complications, preeclampsia, or organ rejection arise late in the second or in the third trimester. If there is a serious threat to the life or health of the mother, the gravid uterus should be removed or the pregnancy terminated. If the fetus is born alive after such a crisis, the parents may be confronted with a premature newborn on the margins of viability and the special burdens which that entails.¹¹ If uterus transplant research shows that early prematurity occurs more frequently after transplant, that fact will directly impact the acceptability of that procedure.

⁵ That principle is that ‘couples (or single reproducers) should select the child, of the possible children they could have, who is expected to have the best life ... based on the relevant, available information.’ Daar & Klipstein, *supra* note 1 at 4, citing Julian Savelescu, *Procreative Beneficence: Why We Should Select the Best Children*, 16 *BIOETHICS* 413 (2001).

⁶ It is unclear that such a duty exists before the studies of uterus transplant now underway in Sweden and the United States and elsewhere are completed. The very point of those studies is to determine whether the risks they allege are so great that surrogacy is always preferable. As noted, however, that position leaves open the question of whether transplant is acceptable if surrogacy is not available.

⁷ *Id.* at 1, 3 and 4.

⁸ *Id.* at 2.

⁹ A person who believes that a human entity with rights exists from fertilization or implantation would disagree with this statement. Some persons who accept abortion might view viability as conferring rights, but in American law constitutional personhood does not attach until a live birth.

¹⁰ The authors assume the availability of surrogacy for anyone undergoing uterus transplant, which I argue below is rarely the case. See *infra* p. 6.

¹¹ For the difficult problems that arise with extreme prematurity, see John A. Robertson, *Extreme Prematurity and Parental Rights after Baby Doe*, 34 *HASTINGS CTR. REP.* 32, 39 (2004).

WHAT ARE THE RISKS OF HARM FROM TRANSPLANT AND SURROGACY?

Daar and Klipstein are concerned that the risks of uterus transplant to the resulting child and mother are so significant that they might contraindicate pregnancy in donor uteruses (at least when surrogacy is available). But are they so great as to disqualify transplant?

They mention two kinds of risk—vascular complications and teratogenic effects of immunosuppressive drugs. No doubt the doctors and ethics committees at the Karolinska Institute, the Cleveland Clinic, and other institutions considering uterus transplant have evaluated such risks, as well as risks to the health and life of the mother (and living donor if one is used). The subjects would also have been extensively counseled, and as in other transplants, would not be accepted as patients unless they fully understood the risks and uncertainties, had a social support system in place, and physicians are satisfied that the risks of transplant, while real, are ethically acceptable. Yet without much more experience—the very purpose of the experimental series now occurring—the true risks of transplant will be unknown.

One set of risks involves the difficulty of successful revascularization of the donor uterus. Only highly skilled vascular surgeons will be able to successfully suture paper-thin arteries and veins. Even then vascular risks such as clotting and impaired blood flow to the placenta and other organs may occur, threatening the life of the mother and fetus/child. Preeclampsia, which occurs in 1 in 2000 births in the developed world, is an ever present threat due to the vascular impairments that could occur after transplant.¹² With early delivery the only treatment in severe preeclampsia, uterus transplant could lead to a higher rate of early premature births and the complications that can follow, including disabilities, epilepsy, cerebral palsy, and hearing and vision problems.¹³ Ongoing and future studies will be needed to determine whether vascular problems will be so great in pregnancy after uterus transplant as to make its use unacceptable.

A second set of risks arises from the effects of immunosuppression during pregnancy. With over 1200 children born to women using immunosuppressive agents after transplant, doctors now have considerable experience in how to plan and manage such pregnancies after transplant so that safe outcomes generally occur for child and mother.¹⁴ Immunosuppressive drugs vary in their impact. Exposure to azithiopine, prednisone, sirolimus, and other calcineurin inhibitors produce fewer birth defects or preterm delivery than mycophenolate products such as mofetil.¹⁵ This enables drugs to be used that are less associated with low birth weight and preterm delivery, so that transplant recipients may give birth.¹⁶

¹² Indeed, the first live birth from uterus transplant in Sweden occurred prematurely due to preeclampsia. Michelle J. Bayefsky & Benjamin E. Berkman, *The Ethics of Allocating Uterine Transplants*, CAMBRIDGE Q. HEALTH CARE ETHICS (2016), DOI: 10.1017/S09633180115000687.

¹³ A great risk to the health of the mother would occur if the preeclampsia is not treated and the severe seizures of eclampsia occur.

¹⁴ Lisa A. Cosica et al., *Immunosuppressive Drugs and Fetal Outcome*, 28 BEST PRACT. & RES. CLIN. OBSTET. GYNECOL. 1176, 1184 (2014).

¹⁵ *Id.*

¹⁶ C. Blume et al., *Pregnancies in Liver and Kidney Transplant Recipients: A Review of the Current Literature and Recommendation*, 28 BEST PRACT. & RES. CLIN. OBSTET. GYNECOL. 1123, 1136 (2014).

In general, physicians have not found that such a 'higher frequency of pregnancy-associated disorders such as preeclampsia, preterm delivery acceleration of hypertension, new-onset diabetes, and newly arising infection' occur in pregnant transplant recipients to bar pregnancy.¹⁷ There is reason to think that the risk of immunosuppression, which is tolerable for pregnancy in liver and kidney recipients, should also be tolerable for recipients in research studies of womb transplant, if not also beyond.¹⁸ If those risks turn out to be more significant than expected, that will be a major factor in counselling against uterus transplant as an accepted therapy.

Finally, one should not be too quick to assume that gestational surrogacy is risk-free. Uterus transplant programs will transfer only one embryo, while many surrogacy programs transfer two, leading to a higher rate of multiples and higher preterm delivery rates than non-surrogate births.¹⁹ Also, surrogates are less closely monitored than are transplant recipients so problems may not be identified early enough to be effectively treated. There may also be conflicts with the surrogate over prenatal testing and whether termination should or should not occur. Most important, surrogacy will involve gestation by a paid stranger with all the medical and social risks which that might entail. Even if surrogacy pregnancies pose less maternal and offspring risk unless twins are involved, the social complications that can arise with surrogacy can also make the parties miserable. If transplant pregnancies pose higher though still acceptable physical risks, should not prospective parents judge whether that increased risk (if established) is more or less preferable than the emotional and social complexity of surrogacy?

PERSONAL VERSUS IMPERSONAL HARM

A main factor in the authors' argument for preferring surrogacy over transplant is their reliance on the duty of procreative beneficence, which is a theory of 'impersonal' not 'personal' harm. If they were relying on a person-affecting theory of harm, they would have to argue that resulting offspring are physically harmed by transplant when they would not be by gestational surrogacy. But that claim would run afoul of the non-identity problem that Derek Parfit has made famous (Are persons injured by uterus transplant if they would not otherwise have been born without that transplant?).²⁰ The child born from a donor uterus will be a different person than the child born from a native one, because different embryos would have been created and transferred in each case. The child born from the donor uterus would not have been born by gestational surrogacy and thus could not be made better off.²¹

An interesting exception to this situation might occur if a womb recipient has already created an embryo and then must decide for health or other reasons to have it placed in her donated uterus or in a surrogate's uterus. In this case, the person-affecting concept

¹⁷ *Id.*

¹⁸ Indeed, the very purpose of the experimental work now being done is to determine whether those risks are comparable.

¹⁹ Kiran M. Perkins et al., *Trends and Outcomes of Gestational Surrogacy in the United States*, 105 FERTIL. STERIL. (2016) (in press). <http://dx.doi.org/10.1016/j.fertnstert.2016.03.050>. However, those risks may be mitigated by transferring fewer embryos given the higher success rates among gestational carrier cycles.

²⁰ DEREK PARFIT, *REASONS AND PERSONS* (1982).

²¹ The only limitation would be if transplant caused such extensive disabilities that its life would not be worth living. If that were the case, there would be a duty to end that child's suffering. Those cases are so rare that no harm would have been done to the child because surrogacy would have led to be the birth of a different child.

of harm would be met because the same embryo could have been born in either uterus (and according to the authors worse off because of the higher risk from gestation in a donor uterus). Yet, this situation seems highly unrealistic. Before creating embryos, the parents will ordinarily have decided on surrogacy or transplant, thus different embryos would be involved.²² An implication of the Daar and Klipstein position is that even if a uterus transplant has occurred, there is a moral obligation to transfer embryos into a hired surrogate instead of the uterus transplanted to receive them.²³

Their reliance on procreative beneficence side-steps this problem because it rests on an impersonal theory disconnected to harm to a particular individual. Although dangerously eugenic in its implications, the principle of procreative beneficence is intuitively appealing, since many persons would rather not have disabled children and would rather live in a world without disability.²⁴ Yet, critics have so battered the theory that it has lost any persuasiveness. Consider Professor Rebecca Bennett's critique:

These intuitions, however, merely tell us something about the preferences people have for their lives and the lives of their descendants. Projecting moral significance onto these preferences forces the introduction of an abstract concept of free-floating harm which is unsustainable and thus the Principle and its objectionable conclusions can be dismissed. Parents clearly have a moral responsibility to provide the best life possible for their children but this does not imply an obligation to produce the "best" children possible. As a result there is no moral justification for putting pressure on individuals to produce the "best" child possible ...²⁵

Of course, the choice is not simply between a person-affecting theory of harm and procreative beneficence. One could rely on other theories, but all of them have problems. Other person (rather than same person) affecting theories would look at the impact on others, such as increased health costs or stress on other family members. But those costs must also take account of the benefits that might be achieved despite the higher risk. Also, to be consistent, if the impact on others is key, why are then women not required to have prenatal tests and condemned for not acting on positive results to prevent the chance of a disabled child for whom others may have to bear the costs?

Appeal to virtue ethics and corruption of an ideal of the parental enterprise is less weighty if the parents are committed to raising the child and the risks of major disabilities are a moderate increase over the risks of assisted reproduction or coital reproduction in otherwise acceptable high-risk circumstances. To underline the point, with womb transplant the parents are seeking to have a healthy child, not to select an unhealthy embryo/child when there are healthy embryos to be implanted. Nor are they engaged in intentional diminishment, such as might occur if a deaf couple wishes to

²² The research protocols for uterus transplant will enroll only women who have created transferable embryos before the transplant occurs. This is to ensure that the transplant will not be fruitless, which could occur if women created embryos after transplant and could not create healthy ones. No one has suggested that a transplant recipient should be given donor embryos.

²³ Or not implanted in her if a surrogate is not available. Such a requirement seems harsh after she has undergone the transplant so that she may gestate. But the transplant burdens that she has already undergone would not in themselves justify imposing unacceptable risks to offspring who could have been born without that harm through surrogacy.

²⁴ Rebecca Bennett, *The Fallacy of the Principle of Procreative Beneficence*, 23 *BIOETHICS* 265 (2009).

²⁵ *Id.* at 273.

alter the genes of a hearing embryo to satisfy the preferences or their community or some eccentric preferences. Most important, in most cases outside the United States they will not practically be able to have a child through surrogacy as an alternative to transplant.

IS GESTATIONAL SURROGACY AN ACCESSIBLE ALTERNATIVE TO TRANSPLANT?

The authors' critique assumes that women with absolute uterine infertility will have a choice between a donated and a native surrogate uterus. For women with the means, this might be the case in the United States and perhaps a few other countries that allow paid surrogacy. Even then paid surrogacy is very expensive, and is unlikely to be covered by insurance as transplant would likely be if found to be safe.

But paid surrogacy is illegal in most countries, including the United Kingdom and Europe, if it is permitted at all. By contrast, in the United States several states permit commercial surrogacy, with for-profit brokers matching surrogates and intended parents, with the surrogates themselves receiving a fee beyond medical expenses. Yet judging from the United Kingdom experience, which allows compensation for expenses, some leeway to pay surrogates. A survey by Surrogacy UK found that 95% of surrogates received compensation, with 68% receiving between £10,000 and £15,000.²⁶ Overall, there is no prior check on the compensation paid. It is usually revealed when the intended parents apply for a Parental Order after the birth of the child and the amount of compensation is disclosed retrospectively. Without more transparency about payments and their legitimacy, there is not the robust market that there is in the United States, and thus not the ease of access to surrogacy for those who have a need for it. Accessibility is further burdened by time constraints in obtaining a Parental Order for the intended parents' legal right to parent the child. If the reform efforts now being pushed by surrogacy advocacy groups succeed, surrogacy may become a more accessible option in the United Kingdom, which could then affect willingness to use it instead of uterus transplant.

In other jurisdictions that permit only altruistic or non-commercial surrogacy, surrogacy is in practice likely to be even less accessible than in the United Kingdom. In those countries with limited access to surrogacy the choice would be to have no genetic offspring and adopt or remain childless or undergo uterus transplant. A greater risk of clotting, preeclampsia, and preterm birth would not alone prevent a determination that transplant was safe if the added risks were comparable to the risks in other transplant pregnancies or within the range generally of acceptability for assisted reproduction and high-risk pregnancy.²⁷ Even if those risks were not within that range, undergoing them to have a genetic child (rather than adopt) would still not harm the child, who would not have been born without the transplant, because surrogacy was not available. The

²⁶ Dr. Kirsty Horsey et al, Report of the Surrogacy UK Working Group on Surrogacy Law Reform, *SURROGACY IN THE UK: MYTH BUSTING AND REFORM* pp. 20–21, 35 (November 2015).

²⁷ Even if the risk to offspring from immunosuppressive drugs in both uterus and other transplants is comparable, there is the claim that uterus transplant is more likely to have clotting, blood flow, or other problems because of the delicacy of revascularization. One must wait to see what the frequency and outcomes of vascular problems in uterus transplant are.

woman choosing uterus transplant when surrogacy is not available is seeking to have and to rear her own genetic child, not merely experience pregnancy.

One response to this point would be to have infertile women seek surrogacy abroad, as many thousands of British and Europeans have done. However, with India, Thailand, Nepal, and the Philippines now banning foreign surrogacy, this option may no longer be available.²⁸ Even if it were, it is expensive and onerous, and often exploits women in those countries. A woman who chooses uterus transplant over foreign surrogacy is not acting imprudently or immorally when instead she chooses uterus transplant that is found to have higher but acceptable risks. Indeed, with domestic or foreign surrogacy so limited the child she produces with the donor uterus would not have existed but for use of that technique, and thus is not harmed even if the risks to the child are greater than would occur with surrogacy.²⁹ Nor has the parental enterprise of having, bonding with, and nurturing one's child been corrupted or violated.

What about in the United States where paid surrogacy is legally available and a thriving option for persons with uterine infertility? If uterus transplant is safe and effective, then outcomes for children born under either method will be roughly equally, or close to it. Even if there are some higher risks to mother and child from transplant, and paid surrogacy is legally available and affordable for the infertile women, a woman might reasonably choose uterus transplant over surrogacy to avoid the ethical and social complications of hiring a surrogate to do her own gestational work. No child will be harmed by that choice, nor family ideals have been violated when she chooses to internalize physical and lifestyle burdens rather than transfer them to another woman for money.

Uterus transplant, however, is burdensome to the recipient (and donor if living). Even if it becomes an established therapy covered by insurance, a woman would not have a moral duty to have a transplant instead of hiring a surrogate. As I argued in the original article, if research shows that uterus transplant is roughly comparable in risks to other forms of assisted reproduction, she might choose to have the transplant if she wishes. Where the risks to offspring are much greater, then transplant will not meet the standards needed to become routine.³⁰

CONCLUSION

I am grateful to Professor Daar and to Dr Kligstein for so cogently reminding us of the importance of vascular and immunosuppression effects of transplant on the resulting child and mother. They are right that these effects should not be slighted by ethics committees, physicians, or commentators who see uterus transplant as a way to help a woman with uterine infertility to have a genetic child. If research shows a high rate of mid- or late-term miscarriage or severe prematurity, that will be an important part of the informed consent process, and indeed, relevant to whether there will be societal acceptance and insurance coverage of uterus transplant.

²⁸ Daar & Klipstein, *supra* note 1.

²⁹ She could go to the United States but surrogacy is so expensive there that may not be practical for many persons with uterine infertility.

³⁰ One might interpret a 'much greater' risk to be more than a moderate increase in the risk of harm to the child. Further specification, however, would be needed of 'harm'. Is it the incidence of certain effects, such as preterm birth, or is it the survival and welfare of the child at 3 years after birth (or some milestone)?

Yet, even if the commentators are correct when gestational surrogacy is easily available, it does not follow that uterus transplant is wrong in other circumstances. Their claim has limited reach because only in the United States and a few other countries is the surrogacy option legally available. Even then it would be an option that many infertile women would not choose due to expense or moral compunction. In most places the choice is not between uterus transplant and gestational surrogacy, but uterus transplant or no genetic child at all. More data is necessary to know the full extent of risks to mother and offspring. However, unless the risks of transplant are so major that it should never occur, transplant should not be barred as a choice for women with absolute uterine infertility.