New frontiers in surgery: the case of uterus and penis transplantation¹

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Various types of organ transplantations are now considered standard procedures: heart and liver transplants lengthen lives; kidney transplants also do so, as well as improving quality of life by reducing or eliminating the need for dialysis. The transplantation of faces and limbs, a more novel set of techniques, improves quality of life without necessarily lengthening or 'saving' lives. An even more recent development is uterus and penis transplantations, which also do not save or lengthen life, but increase reproductive and sexual function and thereby improve quality of life.

This chapter identifies and discusses central ethical issues that are likely to arise in the development of uterus and penis transplantations. These include general issues related to the ethics of surgical research, and specific concerns regarding the rationale of these particular procedures in the context of reproductive and sexual medicine. How should prospective patient-subjects be selected for innovative surgeries? Are these procedures appropriate as treatment for gender dysphoria, or should they be restricted to people whose reproductive and sexual organs have been damaged by illness or accident? Who is most likely to benefit and how are benefit and risks to be judged? What are the alternatives to these transplant surgeries? How should donor organs be sourced? Finally, more broadly, how should we think of these procedures from the perspective of cost-effectiveness – are these expensive, non-life-saving procedures a good use of scarce health resources in light of pressing global needs?

Uterus transplantation and penis transplantation: a brief history

Transplant medicine has made tremendous advances during the last decades. An early milestone was the first successful transplantation of a solid organ, the kidney, in 1956 (Merril et al. 1956; Murray et al. 1960); this was later followed by successful transplantations of other organs, including life-saving transplants of lungs (1963) and hearts (1967) as well as transplants aimed

at enhancing quality of life: hand (Dubernard et al. 1999), abdominal wall (Levi et al. 2003), larynx (Birchall et al. 2006), face (Devauchelle et al. 2006), uterus (Brännström et al. 2010; 2014; 2015) and penis (Bateman 2015).

Uterus transplantation in particular raises distinctive issues about the right to reproduce and the relevance of reproductive ability to health and quality of life. The first uterus transplantation was attempted in Germany in 1931, on Lili Elbe, also one of the first trans women to undergo surgery to modify the anatomy of her genitals, removing the male organs (penis and testicles) and constructing female organs (vagina and labia) in order to confirm her desired gender (an early example of what has come to be called ‘gender confirmation surgery’). Uterus transplantation was performed together with the reconstruction of the vaginal cavity as a final surgical step. Lili Elbe died three months after this surgery because of infection following rejection of the transplanted uterus. After that early attempt, it took more than eighty years for the first fully successful uterus transplantation (leading to a live birth), performed at the Sahlgrenska University Hospital in Gothenburg, Sweden, by a surgical team directed by the gynaecologist Brännström and the transplantation surgeon Olausson (2015).

Penile reconstructions, which raise overlapping issues, were also originally performed in the 1930s, by the Russian surgeon Nikolaj Bogoras (1936). At the time, surgeons reconstructed the penis using a series of operations, harvesting tissues from other parts of the body (originally skin, fat and muscles, later bones as well), shaping them and transposing them into the pubic area to resemble a natural penis. Penile reconstruction has developed in the intervening years, and is typically offered to two distinct populations: ‘cis men’ (i.e. individuals whose ‘male’ gender identity matches the sex and/or gender assigned at birth) whose penis was missing following disease or trauma – say, war injury or botched circumcision; and ‘trans men’ (i.e. individuals whose ‘male’ gender identity does not match the ‘female’ sex and/or gender assigned at birth), some of whom seek anatomical changes to reduce suffering resulting from gender dysphoria. In spite of all the surgical advances and refinements over the past eighty years, an ideal technique for penile reconstruction has not yet been developed.

Surgeons have recently attempted to develop penis transplantation as an alternative to traditional penis reconstruction. The first penis transplantation was performed in China in 2006 on a cis man after traumatic severance of the penis, with the surgery reversed after two weeks due to a negative psychological reaction (Hu et al. 2006). Dr Van der Merwe at Tygerberg Hospital, University of Stellenbosch, in South Africa, performed the first successful penis transplantation in 2014, from a cadaver donor to a male patient who had lost his penis following a failed ritual circumcision; the results have been described as satisfactory, with the patient recovering erectile function, leading to a pregnancy (Bateman 2015). A third operation was performed in 2016 at Boston Massachusetts Hospital, though it is not

yet publicly known whether this instance was or will be successful (Caplan et al. 2016).

Uterus and penis transplantations: innovation, care, research

Uterus and penis transplantations are novel surgical procedures, promising significant benefits to those cis and transpeople who are missing an important part of their genital anatomy. However, much remains unknown about the incidence of risks, and the importance of the benefits of these procedures. Going forward, there is an imperative both to offer clinical benefits to prospective subjects and, so far as possible and permissible, to develop generalisable knowledge about these procedures for the sake of future patients. As novel and largely untested therapeutic modalities, uterus and penis transplantations fit into two overlapping ethical categories: clinical care and research.

First and foremost, at present uterus and penis transplantations are sought for clinical benefit; therefore, they are therapies of a particular kind: what are sometimes called *innovative surgeries*. According to Morgenstern (2006), innovative surgery is a novel approach to an unsolved surgical problem or one that offers a substantive improvement of a pre-existing technique. Uterus transplantation provides a novel surgical means to restore or produce fertility, while penis transplantation promises a substantial improvement over existing penile reconstruction techniques. Uterus transplantation restores fertility in cases of absolute uterine factor infertility (AUI), which is the most significant cause of totally untreatable infertility (Olausson et al. 2014). Currently, there is no alternative that will permit a woman with AUI to carry on a pregnancy and deliver a live baby. Interestingly, to serve this end a uterus transplantation need not involve permanent implantation of a donor organ. Thus, uterus transplantation is the first ephemeral (i.e. lasting for a short time) transplantation type, whereby the transplanted organ is only temporarily engrafted, and is removed after the baby is delivered (Olausson et al. 2014).

Penis transplantation procedures, as therapies, treat disorders of the genitalia, enhancing quality of life after injury by restoring valued functioning such as urinating while standing and penetrative sexual intercourse. Further, in some trans men, penis transplantation may provide a clinically effective treatment for gender dysphoria, a serious condition that, inadequately treated, poses high risks of both morbidity (depression, anxiety) and mortality (via suicide). In both cis and trans men, penile reconstruction (regardless of the surgical methods used) has a large and usually positive impact on the subject's psychological well-being. Reconstruction reduces organ-specific dysphoria (i.e. 'unhappiness and discomfort') in cis men with genital injury or pathology. In trans men, reconstruction can be an effective treatment for gender dysphoria, particularly in combination with other therapeutic approaches (other surgical procedures like mastectomy, hormonal therapy

and psychosocial support) (World Professional Association for Transgender Health 2011). However, there is no consensus in the existing literature regarding the best surgical technique for penile reconstruction (Selvaggi and Elander 2008; Wroblewski et al. 2013).

So far, penile reconstruction has been performed by way of surgical techniques involving various tissues (skin, fat, muscle, etc.) which are taken from one part of the patient's body (forearm, thigh, etc.), shaped into a penis, and repositioned on the pubic area of the same patient. One of the most advanced techniques consists in the use of autologous tissue, the radial forearm flap; however, this usually does not completely fulfil patients' expectations and, as mentioned earlier, it presents a high risk of complications, also leaving the recipient with additional scarring of the donor area (Selvaggi et al. 2006; Selvaggi and Elander 2008; Monstrey et al. 2009; Wroblewski et al. 2013). Figure 4.1 shows the results of a reconstruction with this technique; it clearly demonstrates how the reconstructed penis differs from a typical biological penis; Figure 4.2 shows the residual scar on the donor area. These techniques go under the general name of *phalloplasty*. Specifically for trans men, another surgical alternative is *metoidioplasty*, which consists in the simple enlargement of the clitoris and possibly the reconstruction of the urethra, to create what is sometimes called a 'micropenis'.

All of these types of penis reconstructions have important limitations, particularly as treatments for gender dysphoria. First, none of these techniques

Figure 4.1 Penile reconstruction with radial forearm flap

Figure 4.2 Donor-area morbidity (scarring) following the harvesting of a radial forearm flap for penile reconstruction

is able to satisfy entirely patients' expectations: in metoidioplasty, satisfactory penetrative function is not achievable; in phalloplasty, further surgery is needed to implant a silicone erection device into the reconstructed penis, with additional risks such as infection and extrusion of the erection device. Second, in both cases any observer can recognise that the penis has been reconstructed. Currently, there is no technique that can provide a fully passable penis, and therefore full and seamless functioning in the desired gender identity. Third, other functions such as urinating while standing often require extensive additional 'revision' surgeries, with no guarantee of success. Moreover, in both procedures there is a high risk of complications – the risk of total loss of the reconstructed penis is as high as 2 per cent. In phalloplasty there can be significant donor site morbidity, for example, on the radial forearm. Post-operative recovery typically involves weeks of hospitalisation and many months of rehabilitative therapy.

Due to these limitations, many patients who lack a penis do not attempt reconstruction, instead (in many cases) silently suffering with sometimes severe dysphoria. The existence of this population alone shows that there is a significant health need for improved gender confirmation modalities in trans men, a need which might be met by safe and effective penis transplantation procedures. Nonetheless, so far none of the reported penis transplantation cases have been performed for the purpose of gender confirmation. In spite of some critiques following the first report of penis transplantation in an amputated patient (Dubernard, 2006; Hoebeke et al. 2007), expert reconstructive urologists believe this surgical innovation may offer the best results in penile reconstruction for trans as well as cis men, due to a degree of satisfaction that is currently not available from other

methods (Hoebeke et al. 2007). Among all the candidates for penis transplantation, trans men with gender dysphoria represent probably the largest pool. Loss of the penis in cis men due to injury or illness remains relatively rare – the figures are unclear: 7 per cent of military personnel suffer genital injuries in combat, while penile cancer is reported to have a incidence of between 0.3 to 1 in 100,000; however, these figures account for all penile cancers and genital injuries, many of which may not require total penile reconstruction (Bleeker et al. 2008); gender dysphoria in trans men is much more common, with a prevalence ranging from 1:30,400 to 1:200,000 persons in (for instance) Belgium (De Cuypere et al. 2007). Even admitting that not all trans men would want to undergo genital surgery and might be satisfied solely with hormonal therapy and mastectomy, it is still likely that they would represent a large proportion of the patients seeking penile reconstruction by penis transplantation.

Penis and uterus transplantations, therefore, offer substantial benefits to prospective patients. Complex innovations like these should, however, not be pursued lightly, even if the surgeon expects that the patient will benefit. In the case of innovative surgery, particularly surgery which carries significant physical and psychological risks, standard criteria for risk-minimisation include: (1) sufficient scientific background knowledge on the part of the surgical team, probably involving laboratory experiments conducted before procedures are conducted *in vivo*; and (2) stable and sufficient institutional support, with resources reliably available to maximise the chances of a successful procedure, recovery and rehabilitation. Moreover, and relatedly, it is critically important that (3) these innovative surgeries occur within a context of adequate scientific and ethical oversight (Moore 1970; 2000).

It could be argued that this is particularly important in cases such as penis and uterus transplantation, where many innovative procedures will be, though therapeutic, not *merely* therapeutic: the goal will be both to help the patient, and to develop surgical knowledge which can help future patients.

In order to treat someone effectively, it may be necessary to perform these types of surgery; at the end of the day, these types of surgery may be, for some patients, ‘the best available treatment’. However, these surgeries need refinement: they are far from perfect at present; the judgement that they are in the patient’s clinical interests, therefore, will to some extent reflect a chancy balancing of unknown risks against substantial benefits. But to reduce uncertainty about the risks of these procedures, it is necessary to perform them. This results in a situation that some may regard as uncomfortable: those who receive these types of surgery are to some extent ‘human guinea pigs’. Their bodies are utilised to increase knowledge, to collect data and to perfect surgical techniques, in cases where there is, at least, some doubt about whether this is to their clinical benefit. But, at the same time, these ‘guinea pigs’ are also being treated with what they may regard as the ‘best available treatment’ at this given time. So, from this

perspective any alternative here is morally problematic: either the treatment that the patient may judge as ‘the best available treatment’ is provided, and the patient may be exposed to unknown risks and be utilised as a means to gather further knowledge and perfect these types of surgery; or the treatment is denied, and a dissatisfactory status quo is preserved.

As new procedures, penis and uterus transplantations will expose patients to unknown and possibly large risks. Mere consent may be enough to justify these risks, but it may not – physicians may well have a duty not to offer excessively risky therapies, even if patients want them. Or it may be that early instances of these procedures are so expensive that some broader future benefit must be cited to support the expenditure. If penis and uterus transplantations are justifiable as clinical research, as well as clinical care, then there may be an additional justification for physicians to perform these dangerous and expensive procedures in cases where the benefits do not definitively and obviously outweigh the risks.

We would do well, then, to consider whether uterus and penis transplantation procedures, in the short term, might be justifiable as research as well as therapy. Framing the issue in this way has a number of advantages, not least the existence of well-worked-out ethical frameworks for evaluating clinical research. Emanuel et al. (2000), for instance, provide an especially perspicacious set of guidelines for evaluating proposed research. Interpreting a variety of national and international research ethics documents, Emanuel et al. argue that medical research, in order to be ethical, must exhibit: *scientific and social value* (evaluation of the treatment, intervention, or theory that will improve health and well-being or increase knowledge); *scientific validity* (use of accepted scientific principles and methods, including statistical techniques, to produce reliable, i.e. reproducible, and valid, i.e. credible, data); *fair subject selection* (selection of subjects so that stigmatised and vulnerable individuals are not targeted for risky research and the rich and socially powerful are not favoured for potentially beneficial research); *favourable risk–benefit ratio* (minimisation of risk, enhancement of potential benefits, risks proportionate to the benefits to the subject and society); *independent review* (review of the design of the research trial, its proposed subject population and risk–benefit ratio by individuals unaffiliated with the research); *informed consent* (provision of information to subjects about the purpose of the research, its procedures, potential risks, benefits and alternatives, so that the individual understands this information and can make a voluntary decision whether to enrol and continue to participate); *respect for enrolled research participants* (permitting withdrawal from research, protecting privacy through confidentiality, informing subjects of newly discovered risks and benefits, informing subjects of results of clinical research, maintaining welfare of the subjects).

These categories, we believe, are useful for evaluating innovative uterus and penis transplantation procedures whether or not these are always ‘research’ properly speaking (a question we will not attempt to answer

here). Among them, social value, favourable risk–benefit ratio and fair subject selection are the most controversial in penis and uterus transplantations; in the ensuing sections, we discuss these in detail.

Social value

If penis and uterus transplantations are justifiable, even in part, because of benefits to future patients, then their justification involves exposing some patients to risk for the benefit of others. It is therefore important that early attempts at these procedures are conducted in a manner that has some chance of producing knowledge that is of real value.

Penis and uterus transplantations raise subtle and difficult issues about the nature of the value that would be produced, if these techniques were developed to the point where they are part of the standard of care for conditions such as penile injury, infertility and gender dysphoria. Penis transplantation as restorative therapy after loss or damage to a cis man's penis should be relatively uncontroversial; restoring injured bodies to physiological normality is a long-recognised and much-pursued goal of medicine. The other cases raise much more complex and controversial issues: in the case of uterus transplantation, the value of and rights to fertility; and in the case of penis transplantation for trans men, the importance of gender identity and the nature of appropriate treatment for gender dysphoria. We discuss the social value of uterus transplantation first, before transitioning to questions about the social value of penis transplantation and its risks and benefits.

Altruism, procreation, parenthood and uterus transplantation

The first ethics guidelines for research and development into uterus transplantation were presented by the International Federation of Gynaecology and Obstetrics in 2009 (Milliez 2009; Olausson et al. 2014): considerations adduced include the value of, and rights to, procreation as well as considerations regarding altruism and alternatives such as adoption. Uterus transplantation, unlike penis transplantation, is intended primarily, perhaps exclusively, to allow a single specific sort of bodily functioning: conceiving, gestating and giving birth to a child. This is evidenced by the fact, mentioned above, that transplanted uteruses are removed after successful birth. Thus, it is important to consider the ethics of this procedure in light of the costs and benefits of the alternatives available to those unable to conceive a child with existing fertility treatments.

In general, there are three options for infertility in the absence of a functioning uterus: (1) choosing not to have children; (2) adopting a child; or (3) pursuing gestational surrogacy. A first point about social value is that adding uterus transplantation to this menu of options can, at the very least, be expected to reduce the incidence of alternative choices. The social

value of this eventuality is uncertain, given uncertainty in the magnitude of effects, but it seems likely that widespread availability of uterus transplantation would somewhat decrease the rate of adoptions. Since adoption promotes the well-being of un-parented children, uterus transplantation could be expected to have negative effects in at least this respect, somewhat reducing the supply of prospective adoptive parents. However, the same could be said of any novel fertility treatment; thus, this in itself does not seem to be a decisive objection to uterus transplantation. Moreover, there are serious concerns about the practice of gestational surrogacy, including concerns about exploitation of surrogates (Brännström et al. 2010); any harm done in reducing adoption might be counterbalanced (in whole or in part) by the benefit of reducing the rate of surrogacy and its attendant problems. More recently, Testa and Johannesson (2017) highlight how uterus transplantation offers the mother the possibility of transferring the parental genetic material, and carrying her pregnancy simultaneously.

It might be asked, further, whether restoring fertility – a function that does not seem to be necessary for many people to live fulfilling and happy lives – ought to be a high-priority medical goal in the first place. Of course, many people profoundly value children and family life; however, obviously, bearing children oneself is not the only way to achieve this goal. That said, many people do seem to think that there is a basic human right to procreate (Quigley 2010). Leaving aside, for now, questions about the cost of reproductive assistance relative to other priorities, it does not seem implausible to think that everyone should be able to choose whether to procreate or not. Uterus transplantation promotes this choice in cases where it might otherwise be completely unavailable, thus producing an important kind of social value.

Supposing we grant that there is some general right to procreation, or at least a reason to promote (positive) reproductive freedom, difficult questions arise as to how this right should be realised in people whose gender identity poorly matches the genital anatomy they were born with. One important use of uterus transplantation would be to provide trans women with the opportunity to procreate in a manner reflective of their gender identity.

Sparrow (2008) and Murphy (2014) have discussed whether trans women should be regarded as eligible for uterus transplantation. More specifically, Murphy (2015) considers whether there would be any morally significant reason why trans women, or even cis men, should not be eligible for the same opportunity to gestate as cis women. Noting that other forms of assisted reproduction technology, such as fertility medication, artificial insemination, *in vitro* fertilisation and surrogacy, are regularly offered to both cis women and trans people, Murphy asks why this particular form of assisted reproduction should only be offered for cis women. To be sure, during the early phases of uterus transplantation research, it may make sense to start with cis women, where the procedure is less technically complicated; however, once many of the transplantation issues common to

both sexes have been solved, there does not seem to be any specific ethical justification to preclude attempting uterus transplantation in trans women. To do so would, Murphy argues, be a form of unjustified discrimination.

Sparrow (2008), who is sceptical of uterus transplantation, focuses his arguments on the allocation of research resources, claiming that all publicly funded research should be limited to sex-typical ways of having children. However, if, as Murphy points out, limiting publicly funded research to 'sex-typical ways' of having children results in discrimination between different groups of patients, it is not clear that cost arguments could suffice. The fact that non-discrimination is costly is not obviously or uncontroversially a strong reason to discriminate. Many believe that justice can sometimes override efficiency, requiring us to devote resources in a manner which sacrifices some overall well-being to promote the possibility of equal treatment of equal persons.

Moreover, as Murphy suggests, Sparrow's proposal seems in some ways to prove too much. After all, the statistically typical form of reproduction for human females involves no artificial fertility aids whatsoever. IVF, for instance, hardly seems 'sex-typical'. Should we, therefore, restrict funding for IVF in favour of an exclusive focus on fertility treatments that attempt to restore biologically 'normal' procreative functioning? That is not at all obvious.

Similar concerns may apply to proposals that would limit uterus transplantation based on the idea that our human right to reproduce only covers reproduction in 'species-typical' ways. The idea here would be that the right to reproduce, though possessed by everyone, is possessed in different ways in 'natural-born men' as opposed to 'natural-born women'. Trans women have a right to reproduce, so that argument goes, as males; thus withholding treatments that might allow them to reproduce in female-typical ways does not violate their reproductive rights.

Again, this argument's focus on species-typicality leaves it unable to justify many existing fertility treatments, which, even in cis women, often involve atypical ways of conceiving and implanting an embryo. Perhaps, however, a proponent of this argument would simply agree that IVF is not included under a human right to reproduce, focusing instead on the right to reproduce as the right to have and make use of a healthy, normal reproductive system. This way of understanding the right is, we suspect, too narrow, fetishising arbitrary facts about statistically typical humans and ignoring the importance of simply being able to do important things, however you do them. We would suggest instead a human right to reproduce in a manner consistent with an individual's basic values and sense of identity; a right, therefore, which would imply that there is strong reason to help trans women reproduce as women.

However, even a more restricted conception of the right to reproduce, a right to reproductive health, could justify uterus transplantation in many trans women. This narrower conception focuses on healthy reproduction as

sex-typical reproduction. But health is not just about normality; it is also about the avoidance of suffering. Many trans women suffer from serious cases of gender dysphoria; prior to gender confirmation, they are, therefore, not healthy. Asking them to preserve anatomical structures needed for male-typical fertility until such time as they are ready to bear children is asking them to sacrifice health for reproduction – a demand that ought to be viewed sceptically, on any plausible conception of reproductive rights.

Uterus transplantation as an innovative fertility treatment also opens the possibility of a much more atypical kind of reproduction: uteruses could be transplanted into cis men. This clearly does not solve a health problem; it would, therefore, go beyond the right to reproduce in a healthy way. Even on our broader understanding of the right to reproduce consistent with deeply held beliefs and identities, we doubt that there will often be a forceful claim to uterus transplantation in cis men; it will rarely be the case that a cis man's deeply held values or identity demand that he reproduce by gestating a genetically related child in his own body. Cis men have many other opportunities for socially endorsed, stigma-free parenthood; to most cis men, gestating a child would be at most one option among others. Lacking an option, even if it would be good to have it, is not in itself a rights violation.

That said, one could imagine circumstances under which uterus transplantation in cis men ought to be seriously considered. Murphy (2015) proposes the case of a man who might wish to gestate a child because his female partner is unable to do so (because of uterus incapacity or pregnancy risk to her health) or unwilling to (because she is the main economic provider in the relationship and does not want to lose time to pregnancy). Further, male gestation might appeal to male same-sex couples.

Sparrow worries that, if people identified at birth as male could gestate children, we should be concerned about 'changes in the social meaning and expectations of sexed bodies' (2008: 295). It is, however, hardly obvious that such changes would be a bad thing: feminists have mounted powerful arguments that these meanings and expectations place undue burdens on women (Haslanger 2012). Eventually, offering uterus transplantation in trans women and cis men could provide reproductive options that would be valuable both for the individuals who take advantage of them, and for the structure of the society in which they live. Still, we stress that one need not accept this more radical conclusion to accept a human-rights-based case for uterus transplantation in trans women; that, again, can be understood, in many cases, as a consequence of the right to reproduce free from gender dysphoria.

Risk–benefit ratios in penis and uterus transplantations

There is as yet little detailed discussion of the risks and benefits of penis transplantation in the ethics literature; what there is focuses exclusively on

cis men. The group at the Guangzhou General Hospital in China, where the first penis transplantation was performed, attempted to discuss ethical issues related to this innovative surgery, but they did not discuss penis transplantation specifically for trans patients; their analysis was limited to pointing out the importance of considering risk–benefit ratio, informed consent, fair patient selection and psychological assessment, before proceeding with the surgery.

In one of the few extant discussions of the ethics of penis transplantation, Caplan et al. (2016) assert that the development of penis transplantation procedures in live human beings should pause until ethical guidelines are developed. Since, they maintain, penis transplantation is not a life-saving procedure, but rather a high-risk mode for improving quality of life, a precautionary principle requires that procedures should be halted until explicit ethical guidelines are adopted. Ethical discussion must cover the donation of tissue, consent, subject selection, the qualifications of the surgical team and management of both failure and patient dissatisfaction. Caplan et al. conclude that, unless these issues are discussed in more detail, penis transplantation should not be undertaken. We think that Caplan et al. (2016) underestimate the urgency of the clinical needs that penis transplantation meets, and overstate our present state of uncertainty regarding the risks and benefits of the procedure. Caplan is right that only a few anatomical and animal studies on penis transplantation have been reported in the literature (Sonmez et al. 2009; Zhang et al. 2010; Tuffaha, Sacks et al. 2014; Tuffaha, Budihardjo et al. 2014). However, penis reconstruction as currently practised provides a partial model; and here there are many successful and well-studied cases, particularly in trans men (Selvaggi and Elander 2008; Monstrey et al. 2009; World Professional Association for Transgender Health 2011; Wroblewski et al. 2013). It is our judgement that there is sufficient scientific knowledge regarding the underlying anatomical problems to proceed with transplantation attempts in humans, if this is otherwise ethically permissible.

Caplan et al. (2016) adopt a more cautious attitude, in part, because they draw a sharp distinction between penis transplantation as a very risky ‘life-enhancing’ procedure, which simply improves quality of life, and ‘life-saving’ procedures, as in many cases of solid organ transplant. More recently, Caplan and Purves (2017) have highlighted how candidates for life-improving organ transplantation may have poor judgement when assessing risks and benefits. This raises the possibility that the decision to opt for surgery may not represent a genuine expression of autonomy. However, as Caplan and Purves note, many other life-improving surgeries widely offered today, as reconstructive (as well as cosmetic) procedures, carry a risk of death from anaesthesia or other complications after surgery such as deadly infections, and yet these procedures are widely offered and chosen. Though it is important for patients to understand risks before undertaking dangerous procedures, banning whole categories of procedure on grounds of concern

about misunderstanding of risk goes much further than present practice does or should.

Our view is that all transplants are inherently risky procedures and all carry with them the attendant risks of permanent immunosuppressant therapy (Diaz-Siso et al. 2013; Siemionow 2012). But these risks must be counterbalanced against the benefits, without giving categorical priority to length of life over quality of life. Moreover, it is worth noting that some penis transplantations may extend expected lifespan as well as improve quality of life. For gender dysphoria patients, the degree of dysphoria and subsequent risk of suicide may be so high that adequate gender confirmation might be considered a life-saving procedure.

To be sure, in addition to the risks of immunosuppressant therapy (Siemionow 2012; Diaz-Siso et al. 2013), there are also psychosocial risks, in penis transplantation especially (Caplan et al. 2016). Unlike solid organ grafts (e.g. liver, heart), hand, penis and face transplants are visible, and thus may have more pronounced implications for the recipient's sense of self (Kumnig and Jowsey-Gregoire 2016). This raises the possibility that, as in the Guangzhou case, the recipients would be unable to accept and integrate the graft into their sense of identity and bodily integrity (Carosella and Pradeu 2006). Yet nothing apart from further research in humans could determine whether and to what extent this would actually be the case. In gender dysphoria patients, especially, we believe that post-operative regret will be rare. Significant regret is rare for existing penile construction modalities, even with their many limits. It seems likely that the aesthetic and functional advantages of penis transplantation will produce equivalent or better post-operative satisfaction, though these would have to be weighed against side effects. Still, as Caplan et al. (2016) point out, there will be psychosocial challenges, especially for the early cases, who are likely to receive intense media scrutiny. Caplan et al. are surely right that, *ceteris paribus*, physicians should attempt to minimise these risks as they advise patients about these procedures.

A final issue in risk–benefit evaluation is more fundamental; it concerns the perspective from which risks and benefits should be weighed. One sceptical view on both uterus and penis transplantation might hold that psychosocial benefits, no matter how great, do not justify the enormous risks attendant on complex transplantation surgery and subsequent immunosuppressive therapy. This objection, however, is an anachronism in this anti-paternalistic age of ‘patient-centred care’. Patients seek fertility and gender confirmation procedures because a lack of desired reproductive and/or sexual functioning appears to them, in their own life, as a serious problem. The success or failure of these procedures, particularly in trans populations, is measured primarily, if not exclusively, by self-reported patient satisfaction (Kuiper and Cohen-Kettenis 1988). Clinicians do not and should not decide how big a risk justifies these benefits. They should, of course, advise as to the nature of the risks; when these are high, as in uterus and

penis transplantations, they should take extra steps to ensure that the patient understands them. The same goes, we argue, for surgeons as clinician-researchers, in the development of uterus and penis transplantations. Given the highly personal nature of the goods at stake in uterus and penis transplantations, we should take the fact that well-informed, competent patients are willing to undergo these experimental procedures as reason enough to believe that they have a sufficiently favourable risk–benefit balance.

Fair subject selection: cadaver donors and living donors for uterus and penis transplantations

Uterus and penis transplantations also raise issues of ‘fair subject selection’. That physicians should largely defer risk–benefit judgements to well-informed and competent patients does not mean that many or all prospective patients will be competent and well informed. Moreover, given the risks of this procedure, there may be some limits to deference: patients who are not sure that they themselves will benefit from the procedure, but wish to assist research for the sake of others, might reasonably be refused, given the gravity of the decision to undertake a lifetime of immunosuppressant therapy. Deference to patient judgement on risk and benefit does not entail a totally ‘hands-off’ approach to patient decision. Physicians retain some discretion in restricting their own participation in innovative procedures to cases where the patient can actually expect some benefit. As Caplan et al. (2016) argue, surgeons would be well advised to encourage patients who do understand the distinctive risks of the procedure and who are most likely to benefit. Apart from the physiological and anatomical requirements, personal factors relevant to likely penis transplantation success in cis men might include family and social support, lack of surgical alternatives which could adequately fulfil subject expectations, and strong perceived dysphoria in the preoperative state.

Uterus as well as penis transplantations, as transplant procedures, involve two patients: a donor as well as a recipient. There are also substantial ethical issues about the ‘sourcing’ of uteruses and penises for transplantation. In the uterus transplantation procedures performed so far, surgeons have opted for living donors. The use of a living donor increases the likelihood of success due to higher chance of compatibility (e.g. donation from a relative of the recipient) and ease of procurement; surgery from a living donor can be planned in advance, obviating problems of emergency extraction and transplantation that come along with opportunistic cadaveric donation. Sourcing organs from living donors makes sense in uterus transplantation. Uteruses, unlike many other organs, are sometimes truly ‘surplus’ to the needs of living donors. Some women have no further plans for pregnancy, while others are unable to conceive and gestate a child despite having a healthy uterus. Uterus donation has a risk level similar to hysterectomy,

now a standard procedure (Olausson et al. 2014). Still, recent advances may make dead donor uterus retrieval more feasible in the near future (Testa et al. 2017).

For the cases performed to date of penis transplantation in cis men, surgeons have opted instead for cadaveric donors. It is likely that people would have different attitudes towards the donation of symbolically important organs such as the penis or face, as compared to ‘internal’ organs such as the kidneys, liver and uterus. As Caplan et al. (2016) point out, ‘blanket’ consent to donation, whether actual (‘opt-in’) or presumed (‘opt-out’), may not suffice in these cases. ‘Opt-out’ consent presents particular challenges; it seems implausible to ‘presume’ that people who have never considered organ donation at all would consent to donating such a symbolically important item. Moreover, in both systems, in addition to the deceased person’s wishes, the interests and values of their surviving family should perhaps also be considered (Dickenson and Widdershoven 2001; Roels and Rahmel 2011).

Indeed, it is, at first glance, not entirely clear that the practice of sourcing solely cadaveric tissue for penis transplantation should continue; living donation, if sources could be found, would have the advantage of specific informed consent, along with the other practical advantages discussed above regarding uterus transplantation. It might be thought that living donation would be unlikely, given a dearth of ‘surplus’ penises. This is probably correct, though existing sources should be explored. A small number of cis men suffer from body integrity identity disorder with respect to their penises; if voluntary amputation is permissible in some such cases, this could be one source of living donors (Favazza 1989; Dua 2010). Another, more numerous population (mentioned by the Guangzhou team) would be trans women who seek to be relieved of their male-identified genital anatomy. As it turns out, current gender affirmation surgery modalities for trans women (i.e. vagino-clitorio-labioplasty) require parts of the penis (skin envelope, glans, skin from the scrotum) for the construction of female genitalia (Selvaggi and Bellringer 2011). However, if gender affirmation surgery is developed to the point that penile elements are no longer required to construct the female genitalia, then trans women patients might become a donor source for penises for penis transplantation patients – possibly a particularly apt and psychologically satisfying one for penis transplantation patients seeking treatment for gender dysphoria.

For now, then, it seems unlikely that there will be a significant supply of living penis donors. Cadaveric donors may, therefore, be the only option for penis transplantation procedures in the short term. Though there may be certain practical difficulties in storing and transporting tissues, these do not seem to be decisive, given that all three (somatically) successful penis transplantation operations have used cadaveric donors. Further, given that the only living donors presently available will be patients suffering from

body integrity identity disorder, use of living donors would embroil penis transplantation surgeons in raging controversies about the permissibility of voluntary medical amputation. Thus, for now, cadaveric donation, perhaps with specific consent, appears preferable, while avenues for increasing the quantity and quality of tissue sources for the future are explored.

Uterus and penis transplantation: scarce resources

There is, we believe, a strong case that surgeons would do no wrong to patient-subjects or potential donors when offering and performing uterus and penis transplantations as innovative research procedures. This, however, does not determine whether the development of these procedures is good or just overall. Complex transplant procedures such as uterus and penis transplantations are expensive. Caplan et al. (2016) suggest the costs for penis transplantation could run into the millions; uterus transplantation is very expensive as well, particularly given that, as ‘ephemeral’ transplants, they involve three major procedures – removal from donor, implantation, and later removal from recipient. These procedures, we have argued, could have significant medical benefits in clinical practice. But that is not enough in itself to justify them; these benefits have to be worthwhile, given the costs (Wilkinson and Williams 2016). Resources are scarce, for both research and care, and there are many people in the world who need medical help (Persad et al. 2009). This is true both within health systems that may need to decide whether to cover uterus and penis transplantation procedures, and globally, where large portions of the overall burden of disease are attributable to conditions that can be treated much more cheaply. Moreover, insofar as uterus and penis transplantations are primarily (if not exclusively) life-enhancing rather than life-saving, we might think that they should be deprioritised relative to other expensive transplant treatments, which actually save lives.

It is, in fact, difficult to derive estimates of the likely cost-effectiveness of uterus and penis transplantations, either for cis or trans people. This is in part because the benefits of these procedures are, though probably very real, difficult to quantify and compare to the benefits of other interventions that might be researched or deployed using the same resources. There is in particular little if any systematic work that attempts to quantify the disease burden of gender dysphoria or the cost-effectiveness of various gender affirmation surgery modalities. There is more work on the cost-effectiveness of fertility treatments, though it does not discuss uterus transplantation and covers only cis women (Devlin and Parkin 2003). Still, we would stress a point, presented earlier, that insofar as uterus and/or penis transplantation may constitute the only effective treatment for some severe cases of gender dysphoria, these procedures are likely to have a significant positive effect on both morbidity and mortality in this population, which exhibits high

rates of psychiatric co-morbidity and suicide. Again, the issue is not simply life enhancement vs. life preservation; treatments for gender dysphoria accomplish both.

There is normative uncertainty here, as well. Proponents of cost-effectiveness analysis in global health policy often presuppose a certain sort of ‘consequentialist’ framework, in which relieving a given quanta of health burdens is equally important whoever experiences that burden (Persad et al. 2009). This view puts a strong onus of proof on proponents of any expensive treatment, since the relevant resources can instead be devoted to inexpensive and highly effective interventions in the developing world (e.g. malaria prevention). However, open questions remain about the right of national health systems to prioritise their own citizens over others in the world who might make better use of national health resources. Moreover, even focusing on a given health system, advocates for patients with difficult-to-treat conditions argue that these patient populations should not be abandoned entirely; efforts should be made to develop adequate treatments for every serious health condition, even if some of these conditions are much more expensive to treat than others (Gericke et al. 2005). If any of these arguments are correct, then advocates of uterus and penis transplantations need not show that they are cost-effective relative to, say, malaria prevention in the developing world, or even that they are not much more expensive than treatments offered as standard in developed-world health systems. It may be enough to show that, without access to uterus and penis transplantations, some people – especially some transpeople – will not have an adequate chance at a decent life.

Conclusions

Both uterus and penis transplantation research are ethically plausible when regulated by an ethical framework, though of course many hard questions remain. The benefits of these procedures might include treatment for gender dysphoria in patients who do not see adequate benefits in existing gender affirmation surgery modalities; restoration of normal function in cis populations who have lost penises to injury; and provision of gestational ability in both trans and cis women. Further research is required, however, to understand the magnitude of these benefits and the nature of patients’ normative claims to them. The risks of these procedures are substantial, but patient interest suggests that trans and cis people, as competent evaluators of their own interests, reasonably believe that the benefits justify the risks. Further research will provide more information on the risks of these procedures relative to alternatives, allowing patients to make informed decisions. Organ sourcing raises challenges in both uterus and (especially) penis transplantations, but these do not seem to be insurmountable. Finally, given the global burden of disease, it is important to carefully consider whether

uterus and penis transplantations, as innovative surgery or (eventually) as routine care, are a good use of scarce health resources. Much more research is required here, as well, to understand the cost-effectiveness of these procedures; still, we doubt that cost considerations will or should halt this line of inquiry altogether.

Appendix: terminology

- Absolute uterine factor infertility (AUI): medical condition in which the uterus is absent or diseased, and therefore does not allow normal embryonic implantation.
- Cis man/woman: man/woman whose gender identity matches the sex and/or gender assigned at birth.
- Gender affirmation confirmation surgery: refer to all types of surgery aimed to align the genital anatomy to the gender identity. This includes chest-contouring surgery (e.g. mastectomy in trans men; breast augmentation in trans women), genital surgery (penile reconstruction, or phalloplasty, for trans men; vaginoplasty, clitoro-labioplasty, orchidectomy for trans women).
- Gender dysphoria: distress experienced by a person as a result of the sex and gender assigned at birth.
- Trans man/woman: man/woman whose gender identity does not match the sex and gender assigned at birth.
- Vascularised composite allotransplantation (VCA): also referred as composite tissue allotransplantation, the term used to refer to transplantation of an organ composed of several kinds of tissues (i.e. skin, muscle, bone) such as face, hand, arm and penis.

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