Uterine transplantation: Legal and regulatory implications in the UK

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Abstract

Uterus transplantation (UTx) is fast evolving from an experimental to a clinical procedure, combining solid organ transplantation with assisted reproductive technology. The commencement of the first human uterus transplant trial in the United Kingdom leads us to examine and reflect upon the legal and regulatory aspects closely intertwined with UTx from the process of donation to potential implications on fertility treatment and the birth of the resultant child. As the world's first ephemeral transplant, the possibility of organ restitution requires consideration and is discussed herein. Public funding of fertility treatments pertaining to UTx remains variable and warrants review.

Tweetable abstract

Uterine transplantation warrants a closer look at the UK's legal frameworks on fertility treatment and transplantation.

Key words: Transplantation; uterus; IVF; organ donation; consent; regulation; law.

INTRODUCTION

The last two decades have resulted in the evolution of uterine transplantation (UTx) as a novel method of reproduction. UTx, alongside IVF, presents a transformative option for treating women who are unable to gestate such as those with absolute uterine factor infertility (AUFI) which affects approximately 1 in 500 women of reproductive age worldwide. UTx has ushered in a new clinical arena in the field of transplantation and assisted reproduction. Since the first livebirth following UTx in 2014, women with AUFI may now have an alternative option to adoption and surrogacy in starting a family.[1] To date there have been over 70 UTx procedures and 24 live births achieved, with detailed outcomes from 17 births reported in the literature. This has confirmed UTx as a fast developing medically feasible option.[2] However, being a novel procedure still in its infancy, UTx is undoubtedly associated with significant risk, exemplified by 13 of the first 45 cases (28.6%) resulting in an unplanned hysterectomy.[3] As such, continuous reflection of the alternative options for women with AUFI to acquire motherhood is warranted. Surrogacy and adoption remain the mainstay in such women however neither allow the experience of gestation or childbirth.[2]

Whilst surrogacy allows for biological offspring, it remains forbidden by the law in many countries, or carries restrictions because of ethical or religious views. In the United Kingdom (UK) surrogacy is legal, but commercial surrogacy remains prohibited resulting in a shortage of surrogates.[4] It is also a legally uncertain route to acquiring parenthood, in that the law defines the legal mother as the woman who gestates and gives birth to the child.[5] Furthermore, surrogacy arrangements are not legal binding and not enforceable in the event the surrogate changes her mind after birth.[6]

Adoption can offer legal parenthood but it does not enable biological relatedness. It is also a challenging route to follow, with many initial assessments and vetting of prospective parents, long waiting periods and no guarantee of being matched with a child.[7]

The only therapeutic option which anatomically and physiologically restores the fertility of women with AUFI and allows for biological, legal and social parenthood is UTx. While UTx is not associated with the legal restrictions associated with surrogacy, there are important legal and regulatory aspects that require consideration when commencing a UTx programme. Due to the requirement of IVF and embryo cryopreservation pre procedure, UTx combines assisted reproduction technology with a transplantation procedure, and thus represents a 'new level of collaboration between the two'.[8] This alone may generate regulatory difficulties, since the two fields are regulated differently in many jurisdictions, such as the UK and the USA.

A deceased donor (DD) UTx research programme has commenced in the UK via the 'Investigation Study into Transplantation of the Uterus (INSITU)' trial albeit on pause at the time of writing due to the Covid-19 pandemic. This, along with the exponential rise in the number of successful cases worldwide provokes consideration of the legal issues as UTx transcends from a research concept to a clinical procedure.[9] The legal framework surrounding any medical procedure plays an important role in its successful incorporation into practice. Additionally, development of legal protocols is key for UTx to fit seamlessly with other organ transplants.

The aim of this manuscript is to examine and reflect upon the legal and regulatory aspects closely intertwined with UTx in the UK. It will focus on the process of donation to potential implications on fertility treatment as well as the birth of the resultant child.

Regulation of Uterus Transplantation: square pegs into round holes

UTx is a procedure combining both ART and organ transplantation. In all the research trials to date, conception occurred via implantation of embryos harvested and stored pre-transplant, and implanted once the transplanted uterus was *in situ*. Thus, when the procedure takes place in the UK it will necessitate creation of embryos via IVF. It is therefore anticipated that the procedure will be subject to the regulatory frameworks of both the Human Fertilisation and Embryology (HFE) Act 1990, the Human Tissue (HT) Act 2004 and Human Organ (Deemed Consent) Act 2019. If this procedure becomes a clinical treatment, as it will come under dual regulation, it is important that attention is given to how the procedure can be safeguarded, so as to avoid anomalies of a woman with AUFI seeking to procreate via a UTx and having IVF, only to be later refused access to the UTx procedure. However, should it become possible to allow for natural conception within a UTx setting (although not feasible with the current surgical method), the transplant procedure would presumably fall entirely outside the ambit of regulation designed to govern fertility treatment and the HFE Act /Human Fertilisation and Embryology Authority (HFEA). At present, whilst reproduction via UTx necessitates both a transplant and IVF, both regulatory frameworks apply. As the law governing the latter and access to IVF is well documented[10], the focus of this paper is on the law and regulations that would govern UTx.

Uterus Transplantation

In the UK, if UTx is to be regulated in the same manner as other organ transplants, it would fall under the HT Act 2004 and Human Organ (Deemed Consent) Act 2019, depending on whether the uterus is sourced from a live or deceased donor. The Human Tissue Authority (HTA) is the statutory authority that regulates the removal, storage, use and disposal of human bodies, organs and tissues for a number of scheduled purposes, including transplantation. The rules that would govern UTx will vary depending on whether the uterus is sourced from a living or deceased donor.[11] At present clinical research teams around the world are proceeding using both.

Deceased donation

While the majority of UTx cases to date have involved living donors (LD), the subsequent achievement of livebirths following donation after brainstem death donors has proven the feasibility of UTx using DD's.[12,13,14]

The National Health Service (NHS) organ donor register has over 25 million people registered.[15] In May 2020, following the passing of the Organ Donation (Deemed Consent) Act (2019), organ donation law in England changed to an 'opt out' system whereby adults are presumed to consent to be an organ or tissue donor by default, unless a decision to opt out has been recorded otherwise.[16] As with other rare or novel transplants such as limb and face, donation of the uterus is not included in the opt out strategy and as such, explicit consent is required from the family, close friend or nominated representative of the DD. However, there are challenges associated with making a proxy decision at such an unstable and emotional period. Previously, studies have shown the donation of organs that have not formerly been considered by the deceased individual often result in the grieving family deciding not to

proceed.[17,18] This is reaffirmed by previous studies highlighting prior knowledge of the patients' wishes increases the donor family's willingness to donate.[19 20]

Importantly, the legal position underpinning organ donation is that the state does not own the human body, such individuals that are entitled to determine how their bodily material is used and the donation of organs is considered a 'gift'. Thus, legally valid consent is only relevant if no decision to the contrary has been recorded or expressed by the donor or any qualifying individuals linked to the DD. As such, the donor family will still be approached in all cases and their decision would override the presumed consent associated with the opt out policy.

The principle of consent with regards to the removal of human tissue and organs was made legally binding in 2004 with the introduction of the HT Act 2004.[11] This was following the enquiry that looked in part, at organ retention in Bristol and Liverpool.[21, 22] In these cases, organs of the deceased had been retained without knowledge, or explicit consent from the next of kin.[23] Prior to this, the HT Act (1961) was unsatisfactorily centred on the lack of objection from families, rather than explicit consent with regards to separated biological materials. The HTA was established by the HT Act 2004, to regulate the removal, storage and use human tissue for research, medical treatment, post-mortem examination, education and training, and display in public. The HTA must give approval for organ and bone marrow donations from living people. It was during the non-consensual removal of human 'tissue' that a closer inspection of the difference in the use of terms 'human tissue' and 'organ' was performed.

Vascular composite allograft (VCA) versus a Solid Organ Transplant

The HTA defines an 'organ' as "a differentiated and vital part of the human body, formed by different tissues" and one which "maintains its structure, vascularisation and capacity to develop physiological functions with an important level of autonomy".[24] The definition of "composite tissue" and hence vascular composite allograft (VCA) used by the HTA is a "construct containing multiple structures that may include skin, bone, muscles….that is recovered from a donor as an anatomical or structural unit, without altering its relevant characteristics". Examples given are the face, hand and leg. The launch of the term 'VCA transplant' was initiated with the first successful hand transplant in 1998 and continued to be used for the first face transplant in 2005.[25, 26] Prior to this, composite tissue allograft (CTA) was the term used for reconstructive transplants which were mainly considered tissue transplants, rather than organs. The move to the VCA label for novel transplants displayed recognition of them being more like organs than tissue constructs. The success of VCA transplants as not just reconstructive, but restorative tissues with differing utility, demands an individualised approach to their labelling as a VCA versus a solid organ transplant (SOT).

The functional potential of the human uterus meets the HTA criteria for an organ with it being a vascularised construct consisting of a structured arrangement of tissues and capable of functioning independently of the body (in addition to maintaining a pregnancy). This is proven by the successes of extracorporeal perfusion platforms[27,28,29]. The uterus is therefore more like a traditional SOT yet the transplant community continues to refer to the uterus as a VCA, which has implications for its legal jurisprudence as detailed in this review. [30 31,32] . Recognition of the uterus as a SOT will also drive the development of individualised clinical and service policies and robust training programmes.[33]

Moreover, the standardised scoring system for rejection in a VCA, the Banff VCA system is based primarily on histologic assessment and categorisation into grades 0 to 4. Here, skin is

used as the primary indicator of rejection, whereas in UTx, rejection is based on cervical biopsies.[34,35,36] Therefore, caution must be exercised in the implementation of the Banff schema into clinical practice within the UTx setting. A more applicable classification of acute rejection based on cervical biopsies in recipients of a UTx has been suggested by *Johannesson et al* as displayed in **Figure 1**.[36]

How is a new organ licensed by the HTA?

In the UK, the HTA is the licensing authority for VCAs.[11] The clinical pathway is controlled by the National Health Service Organ Transplant Service (NHSBT) founded upon the NHSBT (Establishment and Constitution) Order 2005. The Multi-visceral and Composite Tissue Advisory Group (MCTAG) works alongside NHSBT to help advise on all aspects of donation and implementation policy.

The HTA also licenses facilities undertaking organ procurement. Removal of the uterus from a deceased individual requires a licence from the HTA. However, a facility storing or transporting the uterus does not require a licence if the person storing it intends to use it for transplantation and it is stored for less than 48 hours.

Although VCAs share a common goal of restorative and life enhancing abilities, they consist of a diverse group of organs with distinct variations in function. The uterus in both its ability and purpose to carry the recipient's reproductive material and amalgamate donor and host utility to form a separate being needs to be considered differently to a 'limb', which is clearly referred to as a VCA. As UTx transitions from an experimental to a clinical procedure, policies in parallel to other SOT's must be considered for its incorporation into practise. This

includes the allocation of DD uterus' which importantly may need to factor the ageing recipient, in addition to regulatory policies on living UTx donors. Furthermore, by recognising the uterus as a SOT, it can assimilate to the same consent policy for organ donation after death. Especially, as unlike VCA transplants such as the face or limbs, there is no physical disfigurement on procurement of the uterus, which involves the same laparotomy incision as made for the procurement of other organs.

Commencing a clinical trial on UTx in the UK has required close collaboration with NHSBT, who coordinate the transplant service. The process required close liaison with a number of committees at NHSBT, including the National Retrieval Group (NRG), the Research, Innovation and Novel Technologies Group (RINTAG) and National Organ Donation Committee (NODC). This is to ensure the plan for the retrieval of the uterus fits seamlessly into the existing multi-organ retrieval process.

The legal status of the Uterus

The legal status of the retrieved uterus remains a debated topic. Whilst ownership is not an issue for recipients of DD organs, it does require consideration for LD UTx. To note however, careful pre-operative interview of the LD is performed, including a psychological assessment to ensure she has securely completed her family and clearly understands donation of her uterus will subject her to terminal gestational infertility. Once the clinical team have deemed the donor medically and psychologically fit to proceed, an independent assessor (IA) is involved to ensure the requirements of the HT Act 2004 are met, and to protect the interests of the donor, particularly in ascertaining no reward or coercion has been sought or offered. The HTA base their approval of the case on the report provided by the IA.

Being the world's first ephemeral transplant, the uterus is exclusive as a transplanted organ in its temporary requirement up until one or two live births are achieved. Beyond this unless a second child is desired, the organ is no longer required and is removed. The possibility of the LD changing her mind after retrieval and requesting the uterus back (organ restitution), perhaps even once it has served its required 'purpose', is one which needs consideration from a legal standpoint. The ethics surrounding the issue of organ restitution have been addressed previously.[37,38]

For UTx, there exists the notion of whether donation of such an organ is a 'loan for use' contract. Human tissue has been recognised as being the subject of property rights by legal scholars in the UK and USA.[39,40,41] Physical detachment of biological material from a human body transforms the material into 'things' which are capable of being the subject of property rights.[42] If applied, property law would assume the uterus as the 'property' of the donor which has been tendered into the possession of the recipient upon implantation and thus the right to ownership rests with the recipient. However, given its temporary therapeutic purpose, the question arises as to whether the uterus is analogous to an implantable medical device for example, where ownership once extracted rests with the surgical team.[43] The HT Act 2004 does not address the legal requirements concerning the removal of materials from living persons, which is governed by common law.

While organ restitution exists as a theoretical possibility for the uterus and as a more probable prospect for the kidney and the heart, a multitude of medical difficulties would prevent safe and efficient re-transplantation.[44,45,46,47,48] This is secondary to deterioration of the organ as a result of surgical implications. Also, the uterine functional ability to carry a further pregnancy would be questionable as empirical data on this is lacking in the field of UTx.

UK law does not currently address organ restitution. Possibly because it has not been considered a serious issue in the past owing to the permanent nature of all other organ transplants performed to date. Although the HTA has clear guidance on the LD's right to withdraw consent prior to the transplant, it does not mention the withdrawal of consent following transplantation. The donor is consented on how they wish to proceed in the event the organ is not implanted into the intended recipient. She is then given four options: for the organ to be transplanted into an alternative recipient on the waiting list or a directed donation, donation to research, disposal, or reimplantation into the donor.[49] Given the HTA states donors have a 'right to withdraw consent at any time *before* the removal of transplantable material', one may deduce the right of ownership is not maintained to the same standard once the uterus is extracted. The decision to proceed with the transplant in the recipient rests with the medical team. No property rights are attached to removed organs as body parts are not presently recognised under property law.[50] Once transplanted, the uterus as any such organ, would require explicit consent from the recipient before removal. With organ restitution, the original recipient would now be treated as a donor under law, thus the same organ donation policies would apply.

Legal implications of the resultant offspring of a UTx

The legal implications of a child born from a donor uterus also needs consideration. Referring to a similar parallel of gestational surrogacy the HFE Act 2008 stipulates the 'woman who is carrying or has carried a child' is the legal mother. That is the case even if the embryo implanted into her contained the gametes of the intending parents. The law does not recognise the sperm or oocyte donor as having any legal right nor responsibility towards the

resultant child.[5] With surrogacy, a parental order would need to be sought by the intended parents after the birth of the child to transfer legal parentage.[5]

Children born as a result of gamete donation can contact the donor at the age of 18. At present, the HFEA does not define the legalities for uterus donors. Given the recipients right of ownership towards the uterus, following donation and subsequent successful fertility treatment, the child to whom she gave birth legally belongs to her if parallels are drawn with surrogacy law. Thus, UTx bypasses the legal challenges encountered with surrogacy and adoption. The donor would have no legal rights over any resulting child.

The DNA of the offspring of UTx recipients will resemble the recipient parents assuming no donor gametes were used. Studies are lacking on whether in the context of UTx there are traces of the uterus donor's DNA in the resultant child. The concept of the uterine endometrium having a reprogramming effect on the embryo has long been suggested.[51] Evidence suggests the endometrial fluid serves as the 'uterine milk' nurturing the embryo.[52, 53] Micro-RNA molecules within the endometrial fluid have been found to be taken up by the embryo resulting in modification of the embryonic transcriptome.[54] This notion of the ability to impart some genetic material to the offspring needs addressing scientifically primarily to draw clear distinctions for the recipient parents and the donor.

Embryo cryopreservation

Embryo cryopreservation is a prerequisite for women undergoing UTx. It is anticipated some time will pass between the recipient undergoing IVF and the UTx procedure. One area which remains tentative is the possibility of withdrawal of consent to the use of the embryos, such as in the event the couple separate.[55] The HFE Act 2008 Schedule 3 stipulates consent for the

cryopreservation and subsequent use of embryos is required by both genetic parents. As such, in the event of a relationship breakdown, if one party withdraws consent the embryos could not be used. Of course, oocyte cryopreservation would deter this risk and allow the recipient more reproductive autonomy. However, despite developments in oocyte storage techniques, cryopreservation of embryos remains the more successful option.[56,57] Given the magnitude of undergoing a UTx, it remains paramount to minimise the risk of fertility failure, therefore embryos remain the preferred option prior to surgery. However, it would be ideal to individualise this depending on each recipient's personal situation.

Funding

Under the trial setting, UTx is funded by the charity Womb Transplant UK for both its procurement and implantation. It is also being offered as a privately funded procedure for LD UTx. With the additional costs of IVF, this unfortunately becomes a polarised procedure towards persons of substantial financial means. Currently, public funding of fertility preservation for women in the UK remains focused on those with compromised fertility as a result of medical treatment. Women with AUFI seeking fertility preservation treatment for the pursuit of a UTx currently need to submit an individual funding request to NHS clinical commissioning groups (CCG's) responsible for managing local budgets. The heterogeneity amongst CCGs funding the provision of fertility treatments across the UK is well known.[58] Correspondence with multiple CCG's has revealed a trend towards declining funding for IVF and cryopreservation for the purpose of UTx due to the principle of cost effectiveness.[59] However, the national commissioning of highly specialised procedures such as UTx is considered directly by NHS England. The decision on whether to fund such a procedure comes from the Prescribed Specialised Services Advisory Group (PSSAG) which advises ministers on innovative treatments not part of existing services. UTx was added to the list of

specialised services in April 2017. Subsequent agreement for funding UTx has received provisional approval by the Secretary of State for Health based on the future results and expenditure of the INSITU study.[60]

A UTx procedure in Europe has been estimated to cost €8,865 for pre-operative investigations and embryo cryopreservation plus €13,800 for costs related to the surgery.[61] This does not include the cost of preimplantation genetic testing which would be necessary for the UK protocol, nor the cost of implantation.

A society which supports individuals to treat infertility through the public funding of IVF treatment should, we may reason, also support the funding of other specialist treatments such as UTx, an additional albeit novel ART. With the costs of surrogacy not entirely clear and the complicated and uncertain route required for the pursuit of adoption, there is a lack of suitable alternatives to UTx. This may provide further justification for the high cost of the procedure in fulfilling this niche healthcare need for women with AUFI.

Conclusion

As the UK's first trial on UTx is underway (albeit postponed), the potential legal implications of a novel organ transplant warrant consideration. UTx represents a combination of a transplant procedure and ART which needs closer inspection under law given the different governing legislation. As the world's first ephemeral transplant, the possibility of organ restitution for LD UTx exists and requires further consideration under law. Legalities for living uterus donors implicating them with the resultant child also need to be addressed. Additionally, given the pace at which UTx is developing into a viable therapeutic option for

women with AUFI, sources of public funding need to consider including women seeking fertility preservation for the purpose of UTx.

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Contribution to authorship

SV and BPJ conceived the idea. SV wrote the manuscript. SS, MF, AA, GT, LJ and JRS provided expertise and helped revise the final draft.

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APPENDIX

Figure 1: Suggested classification of acute uterus rejection in endocervical biopsy samples after uterine transplantation. *adapted from Johannesson et al***.**[36]

Grade	Rejection	Biopsy findings
0	No	Normal morphology
1	Mild	Mild diffuse mixed inflammatory cell infiltrate (mainly lymphocytes) Occasional epithelial apoptotic bodies, focal distribution Surface epithelium intact. No necrosis.
2	Moderate	Moderate, diffuse mixed inflammatory cell infiltrate (mainly lymphocytes) Increased amount of epithelial apoptotic bodies: Reduced thickness surface epithelium, possible focal erosion. No necrosis.
3	Severe	Significant, diffuse and aggregate, mixed inflammatory cell infiltrate (mainly lymphocytes; neutrophils and eosinophils may be present) Frequent apoptotic bodies Epithelial erosions, focal to total Focal necrosis.
4*	Total Necrosis	Necrotic tissue only.

* *Assumed to represent end stage rejection*

REFERENCES

[1] Brännström M, Johannesson L, Bokström H, Kvarnström N, Mölne J, Dahm-Kähler P et al. Livebirth after uterus transplantation. *Lancet*. 2015;*385*:607–616.

[2] Jones, BP, Kasaven L, Vali S, Saso S, Jalmbrant M, Bracewell-Milnes T, et al. Uterine Transplantation; Review of Livebirths and Reproductive Implications. *Transplantation*. 2020; 10.1097/TP.0000000000003578. Advance online publication.

[3] Jones, B. P., Saso, S., Bracewell-Milnes, T., Thum, M. Y., Nicopoullos, J., Diaz-Garcia, C et al. Human uterine transplantation: a review of outcomes from the first 45 cases. BJOG 2019;126(11), 1310–19.

[4] The Surrogacy Arrangeents Act 1985, c.49. [cited 2021 Feb 4]. Available from: https://www.legislation.gov.uk/ukpga/1985/49.

[5] The Human Fertilisation and Embryology Act 2008. c.22. [cited 2020 Dec 21]. Available from: https://www.legislation.gov.uk/ukpga/2008/22/section/33

[6] The Children's Act 1989. c. 41. [cited 2020 Dec 21]. Available from: https://www.legislation.gov.uk/ukpga/1989/41/contents

[7] The Adoption and Children Act 2002. c. 38. [cited 2021 Feb 4]. Available from: https://www.legislation.gov.uk/ukpga/2002/38/contents

[8] Arora KS, Blake V. Uterus transplantation: ethical and regulatory challenges. J Med Ethics. 2014;40(6):396-400.

[9] Jones BP, Saso S, Yazbek J, Smith JR (2016). Uterine transplantation: past, present and future. BJOG 2016;123(9), 1434–1438.

[10] Alghrani A. Regulating Assisted Reproductive Technologies, New Horizons'. Cambridge Bioethics and Law, pp. 275-282. Cambridge; Cambridge University Press; 2018.

[11] The Human Tissue Act 2004. c. 30. [cited 2021 Feb 3]. Available from: https://www.legislation.gov.uk/ukpga/2004/30/section/1

[12] Daolio J, Palomba S, Paganelli S, Falbo A, Aguzzoli L. Uterine transplantation and IVF for congenital or acquired uterine factor infertility: A systematic review of safety and efficacy outcomes in the first 52 recipients). PloS one, 2020:15(4).

[13] Ejzenberg, D, Andraus W, Baratelli Carelli Mendes LR, Ducatti L, Song A, Tanigawa, R et al. Livebirth after uterus transplantation from a deceased donor in a recipient with uterine infertility. Lancet 2019; 392(10165):2697–2704.

[14] Flyckt R, Falcone T, Quintini C, et al. First birth from a deceased donor uterus in the United States: from severe graft rejection to successful cesarean delivery. Am J Obstet Gynecol. 2020;223(2):143-151.

[15] NHS Blood and Transplant Statistics and Clinical Studies, Organ Donation and Transplantation: Activity Report 2019/20, [Internet]. 2020 [cited 2020 Dec 19]. Available from: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/19200/activity-report-2019-2020.pdf

[16] Organ Donation (Deemed consent) Act 2019. c.7. [cited 2021 Feb 3]. Available from: https://www.legislation.gov.uk/ukpga/2019/7/contents/enacted

[17] de Groot J, van Hoek M, Hoedemaekers C, Hoitsma A, Schilderman H, Smeets W et al. Request for organ donation without donor registration: a qualitative study of the perspectives of bereaved relatives. BMC Med. 2016; 17(1): 38.

[18] de Groot J, van Hoek M, Hoedemaekers C, Hoitsma A, Smeets W, Vernooij-Dassen M et al. Decision making on organ donation: the dilemmas of relatives of potential brain dead donors. BMC Med. 2015;16(1):64.

[19] Siminoff LA, Gordon N, Hewlett J, Arnold RM. Factors influencing families' consent for donation of solid organs for transplantation. JAMA. 2001;286(1):71-77.

[20] Siminoff LA, Lawrence RH. Knowing patients preferences about organ donation: does it make a difference? J Trauma. 2002; 53: 754–60.

[21] Dyer C. Bristol inquiry condemns hospital's "club culture". BMJ Clin Res. 2001; 323(7306): 181.

[22] Redfern M. The Royal Liverpool Children's Inquiry Report. London: The Stationery Office, 2001.

[23] Smith R. Regulation of doctors and the Bristol Inquiry. BMJ. 1998; 317:1539-1540. The Royal Liverpool Children's Inquiry Report (The Redfern Report). London: The Stationery Office.

[24] Human Tissue Authority (n.d.) Organ donation and transplant. Available from: https://www.hta.gov.uk/faqs/organ-donation-and-transplant [Accessed 01.09.20].

[25] Dubernard JM, Owen E, Herzberg G, Lanzetta M, Martin X, Kapila H, et al. Human hand allograft: report on first 6 months. Lancet. 1999;353(9161):1315-20.

[26] Devauchelle B, Badet L, Lengelé B, Morelon E, Testelin S, Michallet M, et al. First human face allograft: early report. Lancet 2006; 368(9531), 203–209.

[27] Bulletti C, Jasonni VM, Martinelli G, Govoni E, Tabanelli S, Ciotti PM et al. A 48-hour preservation of an isolated human uterus: endometrial responses to sex steroids. Fertil Steril. 1987;47(1):122-129.

[28] Bulletti C, Jasonni VM, Tabanelli S, Gianaroli L, Ciotti PM, Ferraretti AP et al. Early human pregnancy in vitro utilizing an artificially perfused uterus. Fertil Steril. 1988; 49: 991–996.

[29] Richter O, Wardelmann E, Dombrowski F, Schneider C, Kiel R, Wilhelm K et al. Extracorporeal perfusion of the human uterus as an experimental model in gynaecology and reproductive medicine. Hum Reprod. 2000;15(6):1235-1240.

[30] Honeyman C, Fries CA. Vascularised Composite Allotransplantation – Basic Science and Clinical Applications. Int J Orth Surg. 2019;2(1):13–22.

[31] Rodrigue JR, Tomich D, Fleishman A, Glazier AK. Vascularized Composite Allograft Donation and Transplantation: A Survey of Public Attitudes in the United States. Am J Transplant. 2017;17(10):2687-2695.

[32] Bruno, B., & Arora, K. S. (2018). Uterus Transplantation: The Ethics of Using Deceased Versus Living Donors. AJOB. 2018;18(7):6–15.

[33] Johannesson L, Wall A, Tzakis A, Quintini, C., Richards, E. G., O'Neill et al. Life underneath the VCA umbrella: Perspectives from the US Uterus Transplant Consortium [online ahead of print]. Am J Transplant. 2020;10.

[34] Schneider M, Cardones AR, Selim MA, Cendales LC. Vascularized composite allotransplantation: a closer look at the banff working classification. Transpl Int. 2016; 29(6): 663–671.

[35] Johannesson L, Enskog A, Mölne J, Diaz-Garcia C, Hanafy A, Dahm-Kähler P et al. Preclinical report on allogeneic uterus transplantation in non-human primates. Hum Reprod. 2013;28(1):189-98.

[36] Brännström M, Johannesson L, Dahm-Kähler P, Enskog A, Mölne J, Kvarnström N et al First clinical uterus transplantation trial: a six-month report. Fertil Steril. 2014;101(5):1228-36.

[37] Nakazawa E, Yamamoto K, Akabayashi A, Shaw MH, Demme RA, Akabayashi A. Will you give my kidney back? Organ restitution in living-related kidney transplantation: ethical analyses. J Med Ethics. 2020;46(2):144-150.

[38] Nakazawa E, Maeda S, Yamamoto K, Akabayashi A, Uetake Y, Shaw MH et al Reuse of cardiac organs in transplantation: an ethical analysis. BMC Med. 2018;19(1):77.

[39] Goold I, Skene L, Herring J, Greasley K. The human body as property? Possession, control and commodification. J Med Ethics. 2014;40(1):1-2.

[40] Laslett P ed. Two treatises of government. Cambridge: Cambridge University Press; 1988. p. 287.

[41] Belisle J. Recognizing a quasi-property right in biomaterials. U.C. Irvine L. Rev. 2013;3(3):767–799.

[42] Douglas S. Property rights in human biological material. In: Goold I, Greasley K, Herring J, Skene L, editors. Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century? Oxford: Hart; 2014. p. 89–108.

[43] Dickens BM. Legal and ethical issues of uterus transplantation. Int J Gynaecol Obstet. 2016;133(1):125-128.

[44] Park SJ, Oh SH, Kang MS, Kim TH, Kang SW, Yoon YC et al. Reuse of a previously transplanted kidney from a deceased donor using Luminex virtual crossmatching: a case report. Transplant Proc. 2014;46(6):2083-2085.

[45] Kadambi PV, Chon WJ, Josephson MA, Desai A, Thistlethwaite JR, Harland RC et al. Reuse of a previously transplanted kidney: does success come with a price? Clin Kidney J. 2012;5(5):434-437.

[46] Yıldız S, Çelik A, Camsari T. Long-term Follow-up of a Reused Kidney Allograft. Am J Kidney Dis. 2016;67(6):992.

[47] Copeland H, Gustafson M, Coelho-Anderson R, Mineburg N, Friedman M, Copeland JG et al. Fourth time cardiac Retransplantation. WJPCHS. 2014;5(1):88–90.

[48] Rodríguez-González E, Hernández-Pérez FJ, Gómez-Bueno M, Segovia J, Forteza A, Alonso-Pulpón L. One Heart for Two Recipients: An Effective Option to Increase Donor Organ Availability in Heart Transplantation. Rev Esp Cardiol. 2016;69(12):1220-1221.

[49] Human Tissue Authority. Guidance for transplant teams and independent assessors. Available from: https://www.hta.gov.uk/sites/default/files/HTA-GD-009%20External%20guidance%20to%20Transplant%20Teams%20and%20Independent%20Assessors.pdf [Accessed 15 Nov 2020].

[50] Cronin, A. J., & Price, D. Directed organ donation: is the donor the owner? Clin Ethics. 2008; 3(3):127–131.

[51] Barker D. J. (1990). The fetal and infant origins of adult disease. BMJ Clin Res.1990; 301(6761):1111.

[52] Burton GJ, Jauniaux E, Charnock-Jones DS. Human early placental development: potential roles of the endometrial glands. Placenta. 2007; 28:64-9.

[53] Godfrey, K. M., & Barker, D. J. Fetal programming and adult health. Public Health Nutr. 2001; 4(2): 611–624.

[54] Vilella F, Moreno-Moya JM, Balaguer N, Grasso A, Herrero M, Martínez S, et al. Hsa-miR-30d, secreted by the human endometrium, is taken up by the pre-implantation embryo and might modify its transcriptome. Develop. 2015; 142(18): 3210–3221.

[55] Goodenote E. Evans v. United Kingdom. Cornell Int Law J. 2007; 40:571–88.

[56] Shalom-Paz E, Almog B, Shehata F, Huang J, Holzer H, Chian RC et al. Fertility preservation for breast-cancer patients using IVM followed by oocyte or embryo vitrification. Reprod Biomed Online. 2010;21(4):566-571.

[57] Homburg R, van der Veen F, Silber SJ. Oocyte vitrification – women's emancipation set in stone. Fertil Steril 2009; 91:1319–20

[58] Fertility Fairness. IVF provision in England. Available from: http://www.fertilityfairness.co.uk/nhs-fertility-services/ivf-provision-in-england/ [Accessed 2nd November 2020].

[59] Vali, S. Emails sent to: Care Commissioning Groups across the UK. 10th July – 1st August 2020.

[60] The National Health Service Commissioning Board and Clinical Commissioning Groups (Responsibilities and Standing Rules) (Amendment) Regulations 2020. no.469. [cited 2020 Nov 3]. Available from: https://www.legislation.gov.uk/uksi/2020/469/regulation/1/made

[61] Davidson T, Ekberg J, Sandman L, Brännström M. The costs of human uterus transplantation: a study based on the nine cases of the initial Swedish live donor trial. Hum Reprod. 2021;36(2):358-366.