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THE NEW FRONTIER IN ETHICS AND INFERTILITY: REPRODUCTIVE TISSUE TRANSPLANT, A CASE STUDY OF THE U.S. AND THE U.K.

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Introduction

A little over thirty years ago, bioethicists, lawmakers, and the public alike were engrossed by the birth of Louise Brown and the possibilities that assisted reproductive technology (ART) presented to us. Technologies like in vitro fertilisation (IVF), where embryos are created outside of the body, made it possible for a host of medically infertile, same sex, and single individuals to become parents when they could not have otherwise done so. With the advent of ART came the development of whole markets around gestational surrogacy and egg/sperm donation. These technologies transformed the way we think about reproduction, but they also created countless regulatory and ethical challenges. Scholars, governments, and the public grappled with and continue to be challenged by the issue of where to place ethical and legal limits when it comes to treating the infertile. Issues around who should have access to high-tech treatments, to what extent these technologies should be used and to what end, and whether they are permissible at all, abound. Now the latest advancement in reproductive medicine, reproductive tissue transplant, has come onto the scene, bringing with it great possibilities for the treatment of infertility but even more questions and challenges regarding regulation and ethics. Reproductive tissue transplants, involving the transplant of reproductive tissue like ovaries out of one body and back into that same body or a recipient, may hold the key to treating certain types of infertility, like congenital absence of reproductive organs or cancer-related infertility. However, they raise a fundamental question around what counts for reproduction and what counts as transplantation.

I. Research, Progress, and New Developments

Reproductive tissue transplants currently occupy a range of success dependent on the organ, with some only still being experimented on in animal models while others are showing much success in humans. The most successful reproductive tissue transplants to date are ovarian tissue transplants. The first reported successful live birth after this procedure was in 2004 when a woman, following treatment for non Hodgkins lymphoma, was transplanted with her own previously removed and frozen tissue.[1] In 2005, the first successful *donor* transplant and live birth occurred after the transplant of ovarian tissue between two monozygotic twin sisters where one sister had premature ovarian failure.[2] Two years later, doctors successfully transplanted ovarian tissue between non-identical sisters, paving the way for future transplants that could occur between non-related women.[3] A recent study showed as many as eight live births and two healthy ongoing

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[1] P.J. Donne, *et al.*, 'Live birth after orthotropic transplantation of cryopreserved ovarian tissue', *The Lancet* 2004-9443, pp. 1405-1410.

[2] S.J. Silber, *et al.*, 'Ovarian transplantation between monozygotic twins discordant for premature ovarian failure', *The New England Journal of Medicine* 2005-353, pp. 58-63.

[3] J. Donnez, 'Restoration of ovarian function after allografting of ovarian cortex between genetically non-identical sisters', *Human Reproduction* 2010-25 (10), 3-5

conceptions in a study of twenty-five women with premature ovarian failure or cancer-related infertility and suggested that grafted ovaries could function as long as eight years or greater post-transplant.[4] Demonstrating the survival of the transplant, in 2010 a woman who underwent an ovarian transplant in 2007 gave birth to a second baby from the same transplant and conceived the child naturally.[5]

In addition to ovarian transplants, other reproductive tissue transplants are also proving to be biologically possible. For instance, a man fathered a child post-cancer after a successful testicular transplant in 2001. Uterine transplants have shown some success in animal models, with human studies being planned.[6] Though the cases of ovarian and testicular transplant discussed above have involved tissue from living persons, deceased donor tissue has also been conceived of as a potential resource as well, raising whole new issues around informed consent, as will be discussed later.

Reproductive tissue transplant offers a number of new curative measures for the infertile. Particularly in the context of cancer, the benefits of ovarian transplant are highlighted. First, ovarian tissue transplant opens the door for fertility preservation in adolescents undergoing chemotherapy where harvesting of eggs for traditional IVF and other ARTs is not feasible. Additionally, for fully-grown women, traditional forms of ART may not be possible because the woman does not have time to delay her treatment or is not able to undergo hormone treatments because of her type of cancer, both which preclude harvesting of eggs.[7] Further, adult women who do not have sexual partners can bank ovarian tissue without needing to create embryos. Uterine and testicular transplant could enable individuals without these sex organs - due to congenital, accidental, or disease-related absence - to conceive and, in the case of uterine transplant, gestate their own genetically related offspring. With all the potential and power wielded by the prospect of reproductive tissue transplant, however, issues of appropriate regulatory and ethics governance are also raised.

II. Regulatory Challenges

In addition to the new potential that reproductive tissue transplant holds for the infertile, it also presents a number of new and unique regulatory challenges. The core dilemmas are that reproductive tissue transplants embody characteristics of both transplant medicine and ART, two bodies of medicine which have traditionally been regulated independently. Using two countries health regulatory systems, the U.S. and the U.K., a number of new regulatory issues are raised by this merging of transplant and reproduction, which will need further research and policy focus in the future if reproductive tissue transplant flourishes into standard clinical practice. Among these are foremost which body of regulations and policies should control reproductive tissue transplant whether transplant or ART, issues of consenting to donate for living or deceased donors, payment for tissue donors, and distribution/insurance coverage of transplants.

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[4] S. Silber, *et al.*, 'Duration of fertility after fresh and frozen ovary transplantation', *Fertility & Sterility* 2010-(94) (6), 2191-94.
[5] H. Briggs, 'BBC mother has second child after ovary transplant', BBC News, February 2010, at: http://news.bbc.co.uk/2/hi/8534227.stm (01/18/2011).
[6] G. Vince, 'Man fathers child after testicular transplant', *New Scientist*, February 2001, at: http://www.newscientist.com/article/dn1851-man-fathers-child-after-testicular-transplant.html (01/18/2011); A. Nair, *et al.*, 'Uterus Transplant: Evidence and Ethics', *Ann NY Acad Sci* 2008-1127, pp. 83-91.
[7] T. Woodruff, 'The Oncofertility Consortium- addressing fertility in young people with cancer', *Nature Reviews Clinical Oncology* 2010-7, pp. 466-475.

II.1 Which Regulation Regulates?

Central to the regulatory challenges raised by reproductive tissue transfer is the issue of how to define this potential new field of medicine. Though developed as a high-tech way to treat infertility, like IVF and other forms of assisted reproduction, reproductive tissue transplant inevitably involves some form of tissue transplantation into a human body, regardless of whether the practice is donor or non-donor, or living v. deceased donor. The U.S. and U.K. both have separate regulatory frameworks for transplant and ART, begging the question of where this merger should fall. The U.S. regulates organs under the Uniform Anatomical Gift Act (UAGA) which defines an anatomical gift as "donation of all or part of a human body," thus not distinguishing between reproductive tissue and other organs.[8] Additionally, ART has very little federal-level regulation in the U.S., apart from the Fertility Clinic Success Rate and Certification Act of Congress, which requires fertility clinics to report success rates and embryo usage.[9] While regulation of reproductive tissue transplant would thus likely fall under the UAGA, the lack of special attention to the unique issues raised by reproductive tissue transplant could be problematic from a regulatory and ethics perspective. The procreative nature of reproductive tissues raises new issues which are not dealt with by general transplant medicine. Particularly in the case of donor ovarian tissue transplant, transplant now means procreation of one's own genetic offspring outside of one's body – an issue explored in ART but never addressed by transplant medicine.

In contrast, the U.K. regulates transplant and reproductive issues separately. Transplant medicine is regulated under the Human Tissue Act of 2004, while embryos and live gametes are regulated under the Human Fertilisation and Embryology Act (HFEA) of 1990.[10] The HFEA, because it solely regulates ART and thus not transplant, does not deal with some of the potential issues raised in reproductive tissue transplant, like using deceased person's tissue, seeking consent from the deceased, allocating resources, and matching donors. Moreover, because the HFEA specifically deals with live gametes which are reproductive cells, it is unclear whether ovaries, uteruses, testicles and other whole reproductive organs would meet the definition under the Act. Which regulations are chosen to regulate reproductive tissue transplant have important implications for other aspects of this practice.

Neither organ regulation alone nor ART regulation alone can handle the unique issues raised when the two practices are merged in the form of reproductive tissue transplant. However, models which more closely mirror ART regulation are better equipped to deal with the most important issue that organ transplant does not deal with, the issue of procreative ability in genetic material.

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[8] National Conference of Commissioners of Uniform State Laws, Uniform Anatomical Gift Act, 2006, sect. 2(3), at: http://www.anatomicalgiftact.org/DesktopDefault.aspx?tabindex=1&tabid=63 (01/18/2011), hereinafter UAGA.

[9] Fertility Clinic Success Rate and Certification Act 1992 42 U.S.C. 263a-1 *et seq.*.

[10] Human Tissue Act 2004 Chapter 30; Human Fertilisation & Embryology Act 1990, Department of Health, at: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsLegislation/DH_080205 (01/18/2011).

II.2 Issues of Consent, Payment, and Distribution

In addition to which type of model should regulate reproductive tissue transplant, other issues like how to properly establish the consent of donors, whether to pay donors, and who should receive treatment, are also important and may be affected by the type of regulatory framework chosen. The issue of proper consent is particularly important in the case of donor transplant and is strongly impacted by which regulatory framework is applied. For example, in the case of a deceased donor, the U.S.'s UAGA permits next-of-kin to donate organs even where the individual did not elect donation when alive.[11] Certainly, this raises new issues when one is dealing with reproductive tissue that has the ability to create genetically-related children without the individual's consent. In contrast, the HFEA in the U.K. only permits donation of embryos or gametes through the individual's consent, which is preferable, given the reproductive potential of these tissues v. other bodily tissues like kidney or liver.[12] However, the Human Tissue Act permits next-of-kin donation and, again, it is unclear which would regulate in this circumstance.[13] In the case of live donors of reproductive tissue, issues of informed consent are also particularly cogent. Research discussing informed consent for live donors of other reproductive products, like egg donors, has focused on ensuring that the donor be free from undue influence and understand what use will be made of her donation, while also warning of the risks of commodification and the health risks to the donor.[14]

Reproductive tissue transplant also raises issues of reimbursement or remuneration for donors. Both the U.S. and U.K. forbid sale of other organs, like kidneys and livers. Likewise the U.K, does not permit a commercial market for surrogacy or egg donation and limits reimbursement in egg donation to a maximum of £ 250 ("reasonable expenses incurred (…) in connection with donating gametes or embryos (…) directly linked to the process of donation").[15] However, the issue of increased remuneration for donation is being reviewed by the Human Fertilisation and Embryology Authority (the main government organisation in charge of fertility-related policies in the U.K.) later next year.[16] In contrast, in the U.S., there is a booming market in ART. Though not permitted in all states, there are parts of the country where egg donation and surrogacy have become large commercial markets and donors are paid high sums ranging from a few thousand to as many as tens of thousands of U.S, dollars. Because reproductive tissue transplant involves aspects of both transplant and ART, the U.S. will need to resolve whether reproductive tissue donors are more akin to gamete donors and gestational surrogates where commercialisation has been permitted or organ donors where it has been strictly forbidden.

Issues of distribution are also raised by reproductive tissue transplant. One US organisation cites ovarian tissue freezing as costing $12,000 U.S. dollars

[11] UAGA, supra note 5 at sect. 9(a).
[12] "If no consent is in place, because the person is unable in law to provide it, or is deceased, then the gametes must not be procured, stored or used. The provisions in the Human Tissue Act 2004 which allow next of kin to provide consent to harvesting of other body tissues do not apply to gametes." HFEA, 'Consent to Use and Storage of Gametes and Embryos, Interpretation of Mandatory Requirements 5A', at: http://www.hfea.gov.uk/336.html#guidanceSection3718 (01/18/2011).
[13] Human Tissue Act 2004 Chapter 30, Part 1, sect. 3(6)(c).
[14] M. McGowan, *Oncofertility: Reflections from the Humanities and Social Sciences*, Northwestern University 2010, Ch. 16.
[15] Human Fertilisation & Embryology Authority (HFEA), Payment for donors, Interpretation of Mandatory Requirements 13A, at: http://www.hfea.gov.uk/500.html#guidanceSection4582 (01/18/2011).
[16] HFEA, Donation Review, April 7, 2010, at: http://www.hfea.gov.uk/5605.html (01/18/2011).

for the procedure alone, with storage fees and re-implantation of tissue not being factored in.[17] The U.S. traditionally covers costs of organ transplantation under health insurance plans, though ART is typically not covered or is covered at additional costs. The U.K. covers ART and transplants under their National Health System (NHS) with limitations (such as number of ART cycle) and thus limits and boundaries of coverage would need to be determined. Additionally, because reproductive tissue would likely be a limited resource in the same way that organs are, ethical allocation criteria for prioritisation would need to be determined. While life-saving organs like kidneys and livers are parcelled out mainly based on who needs most urgently, this is a moot issue in reproductive tissue where the procedure is not life-saving and non-emergent. Defining who has a greater need for reproductive tissue transplant and thus the ability to reproduce raises a host of interesting and challenging ethical issues and value judgments, which will also have to be dealt with in the future if reproductive tissue transplant moves forward.

Conclusion

Reproductive tissue transplant is an exciting development in the area of infertility treatments, but it poses new and challenging ethical and regulatory dilemmas. Central to these issues are the hybrid nature of the practice, which contains elements of transplant medicine as well as assisted reproduction. Whether the practice is treated as organ donation or ART poses important consequences for which regulations should apply, and consequently, other issues set forth in these regulations, like how to handle consent, how to distribute and allocate resources, and whether to permit payment of potential donors. Scholars, policy makers, and the public should watch closely as the field of reproductive tissue transplant continues to develop and grow and should be prepared to deal with the unique issues which will be raised if these new technologies develop and become mainstream, as so many of their fellow fertility treatments have in the past.

[17] Fertile Hope, 'Female Reproductive Options' 2007, at: http://www.fertilehope.org/healthcare-professionals/clinical-tools/female_options_v3.pdf (01/18/2011).