ETHICAL CRITERIA FOR UTERINE TRANSPLANT RECIPIENTS & DONORS IN CLINICAL PRACTICE

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LIST OF ABBREVIATIONS

AI – Artificial Insemination

ARTs – Assisted Reproductive Technologies

ASRM – American Society for Reproductive Medicine

CDC – Centers for Disease Control and Prevention

DCD – Donor after cardiac death

DD – Deceased donor

DDUTx – Deceased donor uterine transplant

FIGO – International Federation of Gynecology and Obstetrics

HLA – Human leukocyte antigen

ISUTx – International society of Uterus Transplantation

IVF – *In Vitro* Fertilization

KPDI – Kidney donor profile index

LD – Living donor

LDUTx – Living donor uterine transplant

MRKH – Mayer-Rokitansky-Kuster-Hauser syndrome *(see RKH)*

OPO – Organ procurement organization

OPTN – Organ Procurement and Transplantation Network

OTT – Ovarian tissue transplantation

RKH –Rokitansky-Kuster-Hauser syndrome *(see MRKH)*

Tx – Transplant/transplantation

UFI – Uterine Factor Infertility

UNOS – United Network for Organ Sharing

UTx – Uterine transplant/transplantation

VCA – Vascularized composite allograft

ABSTRACT

Uterine transplants (UTx) are currently being researched as a method by which a woman with uterine factor infertility (UFI) can become pregnant and gestate her own genetically related child. Current criteria for ethically selecting UTx recipients and donors are limited. At its core, UTx is an organ donation being used as an assisted reproductive technology (ART), therefore this thesis will use the considerations and discussions surrounding organ donations and ARTs to inform an assessment of the current ethical criteria for *receiving* a UTx and the ethical criteria for *donating* one's uterus. The discussions of organ donations and ARTs will also help in proposing and assessing potential additions to the criteria for both UTx candidates and donors in clinical practice and in addressing lingering questions involved in the ethical clinical use of UTx such as allocation of uteri and payment for the procedure.

INTRODUCTION

Infertility is clinically defined as the "inability of a couple to conceive after one year of unprotected intercourse". Infertility can be caused by a number of factors including sperm disorders and ovulatory dysfunction. Medical advances have led to many different types of assisted reproductive technologies (ARTs) that have helped couples conceive. However for women with uterine factor infertility (UFI) the only ways to begin or build a family have been adoption or surrogacy, neither of which allow the intended mother to gestate her genetically related child.

Uterine transplantations (UTx) have for a long time been proposed and experimented with as a treatment option for women with UFI. If successful, a UTx would allow a woman with UFI to conceive and gestate a child that is genetically related to her. UTx has advanced through research stages and is currently in the human research phase. Although it has seen medical success and even several live births, there are still many questions that need to be addressed in order for UTx to be considered a viable and ethical clinical option.

At its core, a uterine transplant is an organ donation being used as an ART. Therefore, the considerations and discussions surrounding organ donations and ARTs can provide helpful frameworks to examine UTx. It is important to note, however, that because UTx is *both* an organ donation and an ART, it is in and of itself distinct from both of these procedures individually, and therefore the discussion, justification, and objections will diverge slightly from both.

The overall goal of this thesis is to assess the current ethical criteria for the selection of UTx recipients and donors for clinical practice as well as to propose

additions to these criteria. The first chapter examines the history and process of UTx as well as the history and processes of organ donations and ARTs. Chapter Two uses the discussions of organ donations and ARTs to inform an assessment of the current ethical criteria for *receiving* a UTx and Chapter Three similarly assesses the ethical criteria for *donating* one's uterus. The discussions of organ donations and ARTs will also help in proposing and assessing potential additional criteria for both UTx candidates and donors in clinical practice. Chapter Four then examines lingering questions involved in the ethical clinical use of UTx such as allocation of uteri and payment for the procedure. The final chapter also examines areas of UTx that require further research and discussion.

CHAPTER ONE: UTx as a Organ Tx and an ART

INTRODUCTION

For most of history, a medical diagnosis was something that had to be accepted, rather than something that could be treated and changed. One such issue is infertility. Infertility is defined as the "inability to conceive or carry a child to delivery. The term is usually limited to situations where the couple has had intercourse regularly for one year without using birth control" ("Infertility"). Infertility can be caused by a number of factors, including sperm disorders and ovulatory dysfunction. Previously, couples who faced infertility were resigned to accepting childlessness or left to seek adoption. Medical advances have led to many different types of assisted reproductive technologies (ARTs) that have helped couples conceive; these advances include egg donation, artificial insemination (AI), and *in vitro* fertilization (IVF). Although these ARTs have helped many couples overcome infertility, medicine has not yet been able to find a solution for certain types of infertility (Nair et al. 83). One such form of infertility, generally considered untreatable, is uterine factor infertility (UFI). UFI can be caused by either congenital or acquired factors. Congenital causes may include Mayer-Rokitansky-Kuster-Hauser (MRKH or RKH) syndrome or uterine hypoplasia, both of which cause women to be born without or with underdeveloped uteri. Acquired causes of UFI include fibroids, intrauterine adhesions, or a previous hysterectomy, which may have been due to infection, pelvic disease, postpartum hemorrhage, etc. (Nair et al. 83).

UFI affects a significant number of women. As of 2008 in the United States, 15.4% of women of reproductive age were probably affected by UFI, about 9.5 million total (Nair et al. 84-85). With known fecundity rates in the United States, there are

thousands of women that fall within this category who have an interest in conceiving (Nair et al. 85). Historically speaking, surrogacy and adoption were the only methods by which women with UFI could become mothers (Brännström et al. 607). For some women, these options for becoming mothers are unsatisfactory because they do not allow one to *conceive* and *gestate* one's *biologically related* child (Castanos et al. 65). Although this difference in means may seem insubstantial to some, psychological studies indicate that infertility in general, and as will be discussed specifically an inability to gestate, causes feelings of defectiveness, stigmatization, and loss of identity (Cousineau and Domar 296; Greil 1682). For other women, the options of surrogacy and adoption are insufficient due to moral, religious, or legal reasons (Brännström et al. 607).

Due to the large subpopulation of women that UFI affects, and due to the dearth of adequate reproductive options, uterine transplantations (UTx) have for a long time been proposed and experimented with as a treatment option for UFI. The first UTx was performed in 2000 in Saudi Arabia. Although the procedure was deemed surgically successful, the medical team had to perform a hysterectomy on the transplanted uterus 99 days after the initial surgery (Fageeh et al. 245-251). In 2011 another attempt at UTx was performed in Turkey. This surgery was deemed the "first UTx gaining long-term function" due to the subsequent six menstrual cycles post-surgery. The patient underwent IVF and became pregnant in 2013; however, complications led to a miscarriage. These simultaneous successes and setbacks led to further research that contributed to the first live birth following UTx, which occurred in Sweden in 2013 (Brännström et al. 610-613). In early 2016, the Cleveland Clinic embarked on a research trial meant to provide UTx for 10 women suffering from UFI. Unlike the Swedish research, the Cleveland Clinic

decided to begin their research using deceased donors (DD) rather than living donors (LD), due to what they cite as fewer ethical implications involved with deceased donors, an idea that will be discussed further. They have, however, stated that they desire to expand their repertoire to perform living donor uterine transplants (LDUTx) eventually ("Uterus Transplant: Procedure & Information"). The first of these surgeries, which was the first UTx performed in the United States, was carried out in February 2016 and was initially successful, but similarly to the aforementioned UTx in 2000, required a hysterectomy due to a fungal infection ("Uterus Transplant: Procedure & Information"). Later in 2016, Baylor University began their research on UTx. Similar to the trial in Sweden, Baylor has primarily used living donors, although more recently the Baylor researchers have performed several deceased donor uterine transplants (DDUTx). The living donors used in the Baylor study have been altruistic donors (i.e. strangers to the recipients), whereas the donors in the Swedish trial were mostly known to the recipients (Sifferlin, "4 Breakthrough Uterus Transplants; Brännström et al. 608). In December of 2017, the first live birth following UTx in the United States resulted from the Baylor University trial. This birth was especially significant because it was the first live birth following UTx achieved outside of the Swedish trial. This replicability is an important step in moving this procedure from the realm of research to that of standard treatment (Sifferlin, "First U.S. Baby Born After a Uterus Transplant"). Since it is clear that UTx will continue to be sought as a treatment option for UFI, the ethical implications of this procedure must continue to be discussed.

The ethical discussion surrounding UTx must begin with the discussions and frameworks used in organ transplantations and ARTs. UTx, at its core, is an organ

transplant used as a form of ART. As such, there are many similarities between these two types of treatment that must be examined. However, although there are many similarities, UTx cannot simply be viewed as an ART nor can it be viewed simply as an organ transplant. To begin, I lay out some of these discussions and considerations surrounding organ donation and ARTs here in the introduction. I then use these frameworks in subsequent chapters to examine the ethical issues surrounding *receiving* UTx and the ethical issues surrounding *donating* one's uterus. Once these considerations have been discussed, I examine particular situations under which UTx is a permissible option and then give general recommendations concerning the procedure. In addition to the frameworks and discussions surrounding organ transplantations and ARTs, UTx is also subject to the considerations of research ethics, as uterine transplants are currently being done as part of research studies, rather than as treatments. Some of these research considerations are touched on in chapters two and three as I consider the ethical considerations surrounding recipients and donors, and the fourth chapter delves into some more of the ethical considerations specific to this phase as research rather than treatment.

ORGAN DONATIONS

HISTORY OF ORGAN TRANSPLANTS

Organ transplants (Tx) take place when an organ or a part of an organ is removed from a donor, either from a living person or a recently deceased individual, and placed into another person whose organ is no longer functioning properly ("Living Donor Transplant"; "Kidney Transplant"). Organ transplantations (Tx) were originally

developed and used only in the direst situations, such as patients undergoing regular dialysis, or in patients facing certain death. In these cases, the significant risks that came with the surgery (e.g. infection, rejection, long-term drug therapy, etc.) were justified by the possibility of life (Catsanos et al. 66).

Modern organ transplantation largely had its start with kidney transplants (Doyle et. al 2966). Dr. David Hume had been interested in helping patients with renal failure by transplanting organs into them from deceased patients. Although he and his colleagues had had little success, in 1947 he was able to transplant a kidney into a woman with postpartum renal failure. The transplanted kidney remained functioning until the woman's own kidneys could recover (Howard et. al 6). The first successful kidney transplantation with long-term function was performed in 1954. Dr. Murray headed up a team, including Dr. Hume, in which a kidney was transplanted from Ronald Herrick to his identical twin brother Richard Herrick (Howard et. al 7). Because of the genetic relationship of the brothers, this transplant did not pose a risk of rejection. The eventual development of immunosuppressants later allowed for transplants between unrelated individuals, which was a groundbreaking step in proliferating organ donation. After the transplant, Richard, the recipient, went on to live for 8 more years, while his donor brother lived for 56 more years (Howard et. al 7). This fact helped doctors and thought leaders of the time to conclude that along with the immense benefit that could be provided to the recipient, there seemed to be minimal risk to the donor of living with only one kidney (Doyle et. al 2967).

This same act of weighing of risks against potential benefits is one that still persists in the conversations surrounding organ donations today, especially when

considering the use of LDs. This justification, based on weighing risks and potential benefits, relies on claims of beneficence and nonmaleficence and determining what constitutes a significant enough benefit to justify risks. Beneficence is the obligation or duty to promote the good. Nonmaleficence, on the other hand, is the obligation or duty to not inflict harm (Beauchamp & Childress 150-151, 197). These are commonly held as two obligations of the utmost importance in medical ethics. The idea behind these obligations is that medical professionals should promote good while also avoiding inflicting harm when dealing with patients. With regard to organ donation, there is always a degree of risk placed on a LD, but in minimizing this risk, with a significant enough benefit to the recipient, the transplant can be justified.

EXPANSION OF ORGAN DONATION

Since the initial work of Drs. Hume and Murray, there have been many changes in the medical field that have affected organ transplantation. These developments help inform how organ donation is viewed today and help us assess when it is appropriate to use LDs, a key issue when discussing UTx. With the development of immunosuppressants, the possibilities for organ donation increased dramatically. Immunosuppressants meant that donors and recipients no longer had to be immunologically identical (i.e. be identical twins), which expanded the pool of individuals for whom organ transplants could be a viable treatment (Doyle et al. 2967).

Doctors then began attempting and succeeding in transplanting other organs, such as livers, lungs, pancreases, and hearts from DDs (Howard et. al 7). Just as quickly as these procedures were developed, it became clear that the major hindrance to these

procedures was the procurement of organs (Howard et. al 8). Certain organs, such as hearts, require deceased donors and therefore procurement of the organs relied on defining when organs can be removed and what constitutes death (i.e. cardiac standards of death vs. brain death criteria – see below)(Howard et. al 8). Other organs however, such as kidneys or uteri, can be taken from either DDs or LDs (a similarity that makes kidney donation a key example to use when examining UTx). With kidneys the use of living donors is possible because it is a paired organ; therefore, one can be removed while the other kidney carries on the necessary functions for the body. With the uterus, the use of LDs is possible because it is possible to live without this particular organ.

Although early on there had been instances of LDs used in kidney transplants, once it became possible to use cadaveric donors this method was preferred because there was no risk placed on a donor (Truog 444). However, doctors recognized that kidneys donated by LDs performed better in their transplant patients because the organs did not suffer from anoxia, a lack of oxygen, prior to removal. This realization by doctors, the development of medical technology to keep respiration and circulation functioning in patients whose bodies could not maintain these functions on their own (e.g. mechanical respirators), and the evolution of Intensive Care Units (ICUs), together called the definition of death into question. Whereas for years death could only be determined by cardiac standards (the cessation of breathing and circulation), doctors, lawyers, and politicians began to wonder if there were other relevant criteria for life (Howard et. al 9; Defining Death 3-5). In 1981, the President's Commission for Bioethics wrote the "Uniform Determination of Death Act." This stated:

> An individual who has sustained either (1) irreversible cessation of circulatory and respiratory functions, or (2) irreversible cessation of all functions of the entire brain, including the brain stem, is dead. A determination of death must be made in accordance with accepted medical standards. (Defining Death 2)

With this new definition of death, the organs harvested from DDs (now determined by brain death criteria) did not suffer from anoxia prior to removal, as they would have by previous death criteria. This change not only provided healthier organs for recipients, it also widened the pool of donors considerably. However, even with this change, the supply of organs still did not meet the needs of potential recipients (Marks et. al 1102; Klein et. al 974).

Both LDs and DDs are used today, depending on the type of organ in question. When considering LDs, there are three categories of donations: 1) directed donation to a loved one or friend, 2) non-directed donation, and 3) directed donation to a stranger (Truog 444). Each type of donation carries different ethical questions regarding the fairness of the donation as well as the pressures a donor may feel (Truog 444-446). Each of these issues regarding organ transplantation (living vs. dead, type of living donations, the unmet need for organs, etc.) are issues that I address with particular regards to UTx.

CATEGORIES OF ORGAN DONATIONS

In addition to the changes that have come regarding organ donors, there have also been many changes to the types of donations themselves. After the initial development of kidney transplants, the majority of organ transplants developed were life-saving

treatments in cases where a vital organ, such as a liver, lung, or heart, was given to a patient to extend his or her life. Over time, however, more transplants began to be developed as quality of life transplants, rather than life-saving treatments. Quality of life transplants include kidney transplants, which were of course part of the earliest transplant surgeries, but also now include limb, face, and other transplants (Castanos 66). Limb, face, and hand transplants, although still considered organ transplants, are examples of vascularized composite allotransplantations (VCAs) (American Society of Transplantation: Vascularized Composite Allotransplantations (VCA) Research"). VCAs are transplantations of *multiple* tissues, such as bone, nerve, and skin, as a functional unit. VCAs were only recently recognized as "covered organs" by the Organ Procurement and Transplantation Network (OPTN) in 2014; prior to 2014, they were considered tissues and were subject to different regulations. In December of 2015, genitourinary organs (e.g. uteri) were classified as VCAs because of the life enhancing but non-vital nature of UTx ("List Covered Body Parts Pertaining to Vascularized Composite Allografts").

In each of these cases, justification for the transplant appeals to beneficence just as with life-saving transplants; however, the justification is more difficult due to the fact that the risks of not receiving the transplant are markedly different (i.e. not receiving the organ does not result in a loss of life). Because the outcome of not receiving the organ is not death, it is harder to justify according to an argument of nonmaleficence (the harm that is being avoided is not death), nor is the lowered quality caused by not receiving an organ transplant (i.e. the lower quality is present prior to the potential donation, not due to not receiving it). If a LD is being used, as could be the case in a kidney donation, the

surgery places risks and burdens on the donor. Therefore medical providers must examine their obligations of nonmaleficence to the donor.

When considering quality of life transplants, even though one's life is not at stake, the justification for the surgery is not unimportant. For example, even though a kidney is a quality of life transplant, the burden of regular dialysis treatments prior to a transplant is significant. Patients receiving in-center dialysis must go to the center several times a week and undergo the treatment for three to five hours at a time ("Hemodialysis"). The time intensity of this treatment means that in addition to the physical burdens and discomfort of kidney failure and of the treatment itself, dialysis affects patients' ability to work and live "normal" lives in which they are not reliant on being close to a dialysis center. I mention this to illustrate the fact that a quality of life transplant does not necessarily confer a small or even moderate improvement to someone's life, but as with a kidney transplant, can indicate a vast improvement. Additionally, although quality of life transplants are not immediately life saving, they are often life-extending. For example in addition to the quality of life improvements from a kidney transplant, receiving a kidney, compared to receiving long-term dialysis, results in extending one's life 3-15 years depending on various donor and recipient characteristics (Wong et. al 5).

One common thread throughout many, although not all, of these non-vital transplants, such as hand and face transplants, is a connection to one's identity, which has a similarly vast impact on one's quality of life. UTx is equally connected to a woman's identity, as we will see, yet it is clearly not a life-saving surgery. Although these types of surgeries may in fact confer a significant improvement in an individual's quality of life, it still does not mean that these surgeries are as imperative as life-saving surgeries and

therefore they still require greater justification with regard to beneficence and nonmaleficence.

RISKS OF ORGAN TRANSPLANTS

An organ transplant is a major surgery and as such bears considerable risks. Any surgery is associated with risks of pain, infections, blood clots, wound complications, adverse reactions to anesthesia, and even death. In addition to the immediate surgical risks of receiving an organ transplant, there are the risks associated with the possibility that the patient's body may reject the transplanted organ. Rejection is essentially when the recipient's body recognizes the donated organ as being foreign and thus the immune system attacks the organ as if it were any other entity that does not belong, such as a virus or a bacterial infection. In order to minimize this risk, an organ recipient begins taking immunosuppressants prior to the procedure. These medications essentially limit the strength of the patient's immune system to prevent the immune response directed toward the organ. If the body begins to reject the organ after transplantation, the doctors may administer intravenous (IV) anti-rejection drugs to mitigate the response, or in rare cases the donated organ may need to be removed ("Hand Transplant").

The medications used to prevent rejection of the organ, known as immunosuppressants, have a myriad of side effects, ranging from smaller burdens such as acne and weight gain to larger risks such as infections due to an immunosuppressed immune system, diabetes, and increased risk of cancer ("Kidney Transplant"). Organ recipients must take these medications for the remainder of their lives to prevent

rejection, and thus the associated risks of immunosuppressants are long-term considerations.[1]

Although the aforementioned risks are significant, the risks of transplantation are justified by the potential benefits of the surgery. For life-saving transplants, the potential benefit is obvious, the possibility of extended life span. However, as was mentioned and as will be discussed further with UTx particularly, when the nature of the surgery is *not* life saving, and therefore the surgery and assumption of associated risks is not necessary, the assumption of risk requires stronger justification. The potential benefits in these cases are potential improvements in quality of life and possible a longer life.

Living donors are healthy people willingly taking on medically unnecessary risks in order to confer benefit to a patient in need. These risks include general surgical risks of pain, infection, hernia, bleeding, blood clots, wound complications, adverse reactions to anesthesia, and even death ("Living Donor Transplant"). In addition to these surgical risks, organ donation is also associated with mental health risks involving the procedure itself, the process of deciding to donate, and the pressure associated with the success or failure of the procedure for the recipient (Rodrigue et al. 773-777). The UTx procurement procedure involves the removal of the uterus along with the vessel extensions. When a UTx uses a LD, the organ procurement carries risks of surgical injury to surrounding organs such as the bladder, ureters, or bowel; thrombosis; and early onset of menopause (Kisu et al. 1408-1410). It is also worth mentioning, although it may be obvious, that a living uterine donor cannot become pregnant following the donation.

[1] As we will discuss, the donated uterus is eventually removed after one to two live births following UTx in order to minimize the risks and burdens of long-term use of immunosuppressants.

In addition to these larger risks taken on by donors, there are smaller burdens that they are taking on as well. With organ donation in general, these burdens mostly revolve around the time invested in screenings and evaluations prior to the surgery as well as recovery time after surgery. For example, with liver lobe donations, this is generally a five day hospital stay immediately following surgery and two to three months of recovery time after that before returning to normal work and activity ("Living Donor Transplant"). In the Swedish study, the LDs remained in the hospital for recovery for an average of six days (Brännström 70). Additionally, for a donor who has not already begun menopause, the UTx procedure will begin menopause, which carries its own physical and psychological burdens.

COSTS AND PAYMENTS

One current discussion surrounding the practice of organ donation is how LDs or DDs' families are compensated for the donation. The ethics surrounding the appropriateness of compensation are not examined here, but an overview of the laws is important to later examine how legal and ethical precepts about compensation will be applied to UTx, especially given the vast differences between laws addressing compensation for organ donations and those addressing compensation for ARTs.[2] According to the National Organ Transplantation Act, donors are prohibited from receiving "valuable consideration" for the organ (National Organ Transplantation Act). The laws of organ donation make payment for organ donation illegal, but coverage of certain expenses is permissible. Generally the recipient's health insurance will pay for a

[2] I only examine the laws of the United States.

LD's immediate medical expenses, but the donor cannot be paid for the organ itself. Furthermore, donors often are left paying for travel to and from the various medial appointments and procedures and are not compensated for lost wages due to the surgery (Friedman 746). Many worry that the expenses placed on LDs and their families unfairly burden would-be donors and discourage them from donating. Much of the debate surrounding payment for organs revolves around the possibility that payment for organs would increase the pool of donors and alleviate the length of the waiting list and long wait times for recipients. Those who maintain that payment for organs is unethical often cite two things, both of which are relevant in conversations regarding UTx. One objection to payment is that it will limit access to organ donations to those who can afford to pay exorbitant prices for an organ (Friedman 747). Another argument against paying for organs revolves around the concern that vulnerable populations will be exploited for their organs (Friedman 747). These arguments involving organs, payment, and compensation influence the conversations in chapters two and three as I examine the ethical considerations of donating and receiving a UTx.

While this is by no means an exhaustive history of organ transplantation, nor a complete examination of all of the ethical considerations of transplant surgeries, this lays the groundwork for some of the key considerations still facing organ transplantation today. Many of the same questions come into play when examining UTx. That being said, UTx is both an organ transplant as well as an ART, meaning the answers that may

be found for organ transplantation in general do not always translate directly when discussing UTx.

ASSISTED REPRODUCTIVE TECHNOLOGIES

TYPES OF ARTS

The first type of ART was artificial insemination (AI) –either intravaginal or intrauterine (Shanner and Nisker 1589). Compared to the other types of assisted reproduction, AI is relatively straightforward. A sperm sample from a donor, either anonymous or known, is inserted into either a woman's vagina or cervix; it then travels to the fallopian tube, where it meets and fertilizes an egg in the body's natural process. AI may also be accompanied by ovarian stimulation to increase the output of eggs and thus increase the likelihood of conception (Shanner and Nisker 1589). *In vitro* fertilization (IVF), another type of ART, is a more complicated process, yet it has become widespread option for individuals and couples facing infertility. The basic process of IVF is that a woman's ovaries are stimulated and eggs are retrieved. The eggs are then fertilized *in vitro*, (i.e. outside of the body), and incubated; once the embryos have matured, they are transferred into the woman's uterus through a small catheter passing through the cervix. IVF, encompasses several additional types of infertility treatment, such as using donated gametes (eggs, sperm, or both) and using donated embryos (if both partners have factors contributing to infertility or a couple has had several unsuccessful rounds of IVF)(Kirman 241). In each of these types of ARTs, each parent's genetic relationship to the child is determined by whether or not donated gametes are used; however, none of these

procedures themselves preclude the possibility of a couple having both a genetic and gestational relationship with their child.

Each of the above ARTs allows a woman to gestate the child. For example, even if a donated embryo is used, the embryo can still be transferred into the mother receiving the donation, thus allowing her to gestate the child that will be hers, even if she does not share a genetic relationship with her child. Another type of ART is surrogacy, in which another woman is used to gestate and birth the child. There are two types of surrogacies: traditional surrogacy and gestational surrogacy. Traditional surrogacy is when a couple seeks a woman to gestate their child and the surrogate also acts as an egg donor. In this case, the process of AI is carried out; however, unlike the situation above, the insemination is done to the surrogate rather than to the intended mother. This means that the surrogate is both genetically and gestationally related to the child. Gestational surrogacy, more commonly used today, is when the surrogate is not genetically related to the child. In this case, the intended parents use an egg either from the intended mother or an egg from an egg donor (different from the surrogate) and carry out the process of IVF, described above, on the surrogate. As noted, surrogacy can, depending on a couple's type of infertility, provide the intended parents with a child genetically related to them. The primary feature that distinguishes surrogacy from other ARTs is that the woman gestating the child is not one of the child's intended parents.

Adoption, although not an ART, also bears mention here as another reproduction alternative. For couples facing infertility, adoption is an option in which the adopted child is neither genetically nor gestationally related to the adoptive parents. Within adoption there are several routes a couple (or individual) can take to parenthood. Adoption can be

international or domestic, and can be pursued independently, through an agency, or through the foster care system. This is not an exhaustive look at the types of adoption, but the intricacies of adoption lie outside the scope of this thesis. As when two sets of donated gametes are used with a surrogate, the parents are not biologically related to the child, and the intended mother did not gestate the child. Another difference between ARTs and adoption is that women who become pregnant with the help of ARTs, or those who use a surrogate, typically bring home a newborn baby. This often is not the case in adoption, however. In most cases the child is still young, and perhaps even a baby, but unlike the surrogate example given, finalization of adoption does not always happen at birth.

Each of these reproductive alternatives results in the hopeful parents having a child. However, each type of reproductive option has particular drawbacks depending on the specific goals of the parents. As of now, UTx is only permitted to help women with UFI achieve the specific goal of allowing the intended mother to gestate her genetically related child, as set forth in *The Montreal Criteria for the Ethical Feasibility of Uterine Transplantation* (Lefkowitz et al., "The Montreal Criteria"). As mentioned, the only reproductive options currently for women with UFI are surrogacy and adoption, whereas UTx could open up other means of reproduction.

LEGAL SITUATION

One reason many cite UTx as a necessary option to be researched is the moral and legal difficulties women with UFI face when seeking to build a family. Surrogacy and adoption are currently the only options for becoming a mother, for women with UFI.

Each of these options is accompanied by various legal hurdles, which are intended to protect the best interests of the children involved. These legal hurdles, however, often cause uncertainty for the individuals or couples seeking to become a parent through the use of adoption or surrogacy, which can lead to apprehension towards these options. Two court cases exemplifying the legal uncertainty of surrogacy are *In Re Baby "M"* and *Johnson v. Calvert* (Hammons 273-275). In the case of Baby M (1988), a traditional surrogate was used who, after the birth of the child, tried to claim parental rights due to her genetic and gestational relation to the child. When the case was eventually brought before the Supreme Court of New Jersey, the surrogacy contract, which stated that the surrogate would give all parental rights to the intended mother, was invalidated. The adoption of the baby by the intended mother was voided and the surrogate was given visitation rights (Dolgin and Shepherd 219; Hammons 273-274). In *Johnson v. Calvert* (1993), a gestational surrogate was used, but both sets of gametes were from the intended parents. As in the Baby M case, the surrogate attempted to claim parental rights to the child due to her gestational relationship to the child. In this case, however, the genetic relationship the intended parents had to the child was found to outweigh the gestational relationship, therefore her claim was denied (Dolgin and Shepherd 218). The court defined the intended mother as being the woman "who intended to bring about the birth of the child that she intended to raise as her own" ("Surrogate Contract: Parentage" 240). The Supreme Court of California therefore determined that the intended mother was the individual most appropriately treated as the "natural mother."

There are many more court cases that examine the status of motherhood with regard to ARTs. While surrogacy contacts can be drafted before the surrogacy process

begins, the strength of enforceability of these contracts has differed depending on the state and the facts of the case. Additionally, the laws in various states differ greatly according to how "surrogacy-friendly" they are; in some states, surrogacy contracts are wholly unenforceable and laws exist criminalizing compensation for surrogacy. This means that for many women with UFI, although surrogacy is theoretically an option, the legal tenuousness of the situation detracts from its appeal and can even exclude it entirely.

Adoption, on the other hand, has a more forthright and consistent legal system surrounding its process, although the process, laws, and timeline can vary greatly depending on the state you live in, the state or country you are adopting from, the type of adoption you are seeking, and the health status of the child ("Adoption Consent Laws by State"). Although there is less uncertainty about legal and parental status questions in adoption, the process can be restrictively burdensome for certain couples and individuals. The initial part of the adoption process involves a home study in which the parents undergo a thorough background and character check as well as visits to the intended home (National Adoption Center). Potential parents can be denied by an agency based on a variety of factors including their socioeconomic status and age. Even if a couple is approved for adoption in the home study phase, it can still take years to complete the process (National Adoption Center). As mentioned, the legality of adoption, at least in the United States, is not in question; however, this does not always mean that adoption laws always favor adoptive parents. For example, statutes in states like Hawaii, North Dakota, and New Hampshire allow the birth parents to revoke consent for adoption if revocation is found to be in the best interests of the child ("Adoption Consent Laws by State"). This

does not simply mean that if the birth parents attempt to revoke their consent they will be allowed to do so by the court; however, that uncertainty is unsettling for prospective adoptive parents. For some couples, therefore, either the specific adoption laws in their state or the cumbersome nature of the process may make adoption an undesireable or unattainable option, just as with surrogacy.

The precarious nature of both of these reproductive alternatives, either legally or emotionally, is part of the reason that women with UFI optimistically look to UTx. While there are other uncertain aspects to the procedure and surrounding process that I discuss later, on its face, UTx seems to promise an option that is more legally straightforward and that leaves the parental status of the intended parents clear.

BURDENS OF REPRODUCTION

Pregnancy and birth in and of themselves involve risk. Risks during pregnancy can range from issues like anemia, nausea, and hypertension to hemorrhaging, emergency hysterectomies, and even death during the birthing process. The CDC (Centers for Disease Control and Prevention) found that in 2013, the rate of pregnancy related death was 17.3% in the United States (CDC, "Pregnancy Mortality Surveillance System"). The CDC defines pregnancy-related death as "the death of a woman while pregnant or within 1 year of the end of a pregnancy –regardless of the outcome, duration or site of the pregnancy–from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes." (CDC, "Pregnancy Mortality Surveillance System"). Additionally, in 2015 32.0% of all births were *cesarean* sections (c-sections),

meaning those women underwent the additional risks of undergoing surgery and regional or general anesthesia (CDC, "Births- Method of Delivery").

With ARTs involving gestation by the intended mother (e.g. AI or IVF in the intended mother), there are certain additional burdens and risks. The first step of many of these ARTs is to undergo ovarian stimulation to increase the likelihood of success. This step involves some relatively minor burdens as well as some greater risks. Women who ceased IVF treatment cited the psychological toll of the process as well as the daily burden of injections as the primary reasons for desisting with treatment (Fertility & Sterility e62-e63; Fertility & Sterility S263). Although doctors seemed to feel that the ultimate achievement of a birth from this treatment would outweigh these daily burdens of ovarian stimulation, the women involved measured the weight of these burdens differently (Fertility & Sterility S263). In some women, these initial steps involving hormone treatments, for either AI or IVF, can even lead to ovarian hyperstimulation syndrome, which can result in a myriad of symptoms including enlarged ovaries and abdominal pains (Zollner and Dietel 18). After the initial steps, if pregnancy is achieved, IVF also has an increased risk of multiple pregnancies, which in turn carries greater health risk for the mother during pregnancy and labor ("ART and Multiple Births"; "Complications of Multiple Pregnancy").

With a natural pregnancy and birth, or with ARTs involving gestation by the intended mother, these risks are placed on the intended mother herself. When a surrogate is involved, however, some of these burdens and risks are placed on another individual. If the intended mother's eggs are used to create and embryo that the gestational surrogate will carry, then the intended mother faces the risks associated with hormone treatment,

ovarian stimulation, and harvesting.[3] If an egg donor is used and the intended mother goes through IVF, the egg donor takes on the risks and burdens of hormone treatment and ovarian stimulation in order to harvest her donated eggs. With varying degrees, however, these burdens are accepted by the donor or surrogate. It is important to note that the risks and burdens of hormonal treatment, gestation, and birth are placed back on the intended mother in UTx.

COSTS AND PAYMENTS

The laws addressing reproductive compensation are dramatically different from the laws surrounding compensation for organs and organ donation. The debate regarding the ethics of compensation for assisting in reproduction (e.g. donating sperm, donating eggs, acting as a surrogate) are beyond the scope of this thesis, however, the state of this debate and the laws involved influence discussions of UTx donors and recipients and thus the current state of the laws as examined here.

Payments for gametes (sperm and eggs) are routine and generally acceptable. Compensation for sperm is generally uniform. Men are usually paid the same rate, about $50 to $100 per donation, regardless of donor (Almeling 37). The compensation for eggs, on the other hand, varies more. In 2007, the national average for compensation for an egg donor through a clinic was around $4,200 (Covington and Gibbons 1002). This ranged from the lowest payment at $1,500 to the highest payment of $15,000 (Covington and Gibbons 1002). There are also stories of online advertisements or fliers on college campuses seeking "elite" egg donors for a price tag of $25,000 or even $50,000

[3] If a traditional surrogate is used with AI, the additional risks of IVF such as multiple pregnancies are not applicable.

(Covington and Gibbons 1001). Although these high prices are cited both officially and unofficially, the American Society of Reproductive Medicine (ASRM) recommends that payments above $5,000 require justification and states that any payments above $10,000 "go beyond what is appropriate" ("Financial Incentives in Recruitment of Oocyte Donors", S243). They justify this stipulation with the argument that any payments above this amount constitutes an undue inducement, which would lead to recruitment and potential exploitation of vulnerable populations. Rather than eliminating payments altogether, however, ASRM argues that keeping the compensation is imperative to help women understand the real physical and emotional risks and burden that need to be considered when deciding to donate ("Financial Incentives in Recruitment of Oocyte Donors", S241).

Compensation for surrogates involves similar arguments of exploitation, vulnerable populations, and undue inducement. As previously stated, laws about surrogacy vary state by state. Federally, there are no laws pertaining to the enforceability of surrogacy contracts nor are there laws forbidding compensation of surrogates (Watson 532). On a state level, the laws involving surrogacy contracts and compensation vary greatly. Some states expressly forbid any type of compensation to surrogates, meaning that the vast majority of surrogates are family members who are willing to undergo the process of their own goodwill (Watson 533-539). Other states do not expressly forbid compensation; however, any type of compensation would render the surrogacy contract unenforceable (Watson 533-534). These laws and arguments around compensation for gametes and surrogates indicate some of the discussions to be had with regard to UTx donors as this procedure moves out of the realm of research.

REPRODUCTION AND THE UNDERSTANDING OF WOMANHOOD

The idea of womanhood is intricately tied to the idea of motherhood. For many women, their self-identity is deeply connected with their status as a mother or their inability to become a mother, making infertility particularly burdensome emotionally. In a review of the literature on the psychological effects of infertility, eleven themes emerged. These themes are:

1. Infertility as a central focus for *identity*, especially for women.
2. *Feelings of loss of control* and attempts to regain control.
3. *Feelings of defectiveness and reduced competence*, especially for women.
4. *Statuslessness* and ambiguity.
5. *Stress on marital and sexual relations* at the same time that there exists a counter-tendency for infertility to "pull couples together."
6. Feelings of *alienation from the "fertile world*."
7. A sense of *social stigma*.
8. Difficulty dealing with infertility at the *level of meaning.*
9. *Immersion* in the treatment process.
10. Stressful nature of *the treatment process* itself.
11. *Strained relationships with healthcare providers*.

(Greil 1682)

The distress that is caused by this link between womanhood, motherhood, and infertility, although not quantitatively measurable, presents very real issues that need to be addressed when assessing the risks of harm and potential benefits of UTx. The severity of these psychological effects was seen in a study examining depression in women with infertility, in which "11.0% of infertile women met the criteria for a current major depressive episode, compared with 3.9% for the fertile women" (Cousineau and Domar 295). Additionally, 13% of women "experience passive suicidal ideation after an unsuccessful IVF attempt" (Cousineau and Domar 296). In cases where infertility is overcome by ARTs, women still often feel "other" from those who achieve pregnancy

naturally (Kirkman 242). For some women these psychological and emotional effects of infertility persisted even after a pregnancy and live birth was achieved (Cousineau and Domar 297).

It is important to examine these psychological effects prior to addressing the reasons why a woman may opt to pursue UTx, because they provide insight into reasons why many women with UFI do not feel that adoption or surrogacy provides an adequate answer to their infertility. Additionally, these psychological effects should be considered when assessing the success of UTx as a fertility treatment (i.e. Does UTx offer the anticipate psychological benefit when used as a fertility treatment?). As we will see, UTx can easily be viewed by some as simply a preference toward a particular type of ART, a claim we will examine closely. However, I think that the experience that UTx can potentially provide as a fertility treatment (i.e. experiencing pregnancy) may combat some of the psychological effects mentioned in a different manner than surrogacy and adoption can. Although the question of whether this is significant enough to justify pursuing UTx remains, the prevalence and seriousness of these psychological effects need to be examined in full in order to begin to provide a justification.

ARTs (and adoption) share the same general purpose as UTx, to have a child, and in many cases to have a biologically related child. As previously mentioned, with the current criteria set forth in *The Montreal Criteria for the Ethical Feasibility of the Uterine Transplantation*, UTx falls within a particular subset of these reproduction alternatives that fulfill the more specific desire of *gestating* one's genetic child; for

women with UFI, UTx is the only ART within that subset (Lefkowitz et al., "The Montreal Criteria").[4] Even with the similarities between the purpose of ARTs, adoption, and UTx, one distinction is the associated risks and burdens of the three options.

As UTx is a novel procedure, we do not yet have a full picture of its associated risks, a topic that will need further research as this treatment develops. Despite our imperfect understanding, there are certain known and presumed risks. One associated risk is the degree of invasiveness of the procedure. Although most ARTs have a certain degree of invasiveness, UTx possibly requires one or two individuals, depending on whether a LD or a DD is used, to undergo surgery, which introduces new risks as it involves the use of general anesthesia. However, while surrogacy places the burden and risks associated with pregnancy on another individual (not the intended mother), UTx places the risks of gestation solely on the intended mother.

Another associated risk is the recipient's long-term use of immunosuppression. Although this risk is mitigated by the eventual removal of the donated organ, and although this risk is not entirely unfamiliar as it is a risk associated with organ donations in general, this risk still cannot be ignored as UTx is explored as a potential standard treatment.

A final risk that needs to be assessed when examining UTx is the potential risk to future children. Although there have now been live births achieved in two of the research studies, the long term effects on the children have not yet been studied. As UTx moves from research to accepted treatment, there will need to be long-term studies of the mothers and children involved in UTx.

[4] This understanding of UTx only being used to help women have a child that is genetically related to them may eventually change, a consideration that is addressed in the final chapter.

ARTs help provide some initial understandings of a woman's and society's concept of motherhood and even the definition of womanhood. Many of these understandings carry over directly when addressing UFI; however, there are particular distresses facing women affected with this type of infertility. These factors need to be examined closely when discussing recipients of UTx and the appropriate uses of the procedure.

UTERINE TRANSPLANTATION BACKGROUND

To inform our ethical discussion of UTx and its donors and recipients, one must have a basic understanding of the process. If a woman has, at the start of the UTx process, functional ovaries, the first step is for her to have her eggs harvested using ovarian stimulation. These eggs are then fertilized via *in vitro* fertilization (IVF) and the embryos are saved. Based on the current criteria, if a woman does not have functional ovaries, UTx is not a permissible option, as it is restricted to use with a woman's own genetically related embryos. However it is not implausible that UTx will be expanded in the future to be used by women without functional ovaries. If this becomes true, then an egg donor will have to be used; the process for egg donation is the same as with other ARTs. The next step, if a woman has a non-functional uterus still in her body, is to have a hysterectomy to remove it. If a woman does not have a uterus in her body (e.g. if she previously had a hysterectomy or was born without a uterus), this step obviously does not need to occur. If an LD is used, she then undergoes a retrieval surgery to remove her functional uterus and its vessel extensions. In the Swedish trial, the complicated retrieval surgery took from 10.5-13 hours, with an accompanying 6-day hospital stay (Brännström

70). After this, the actual organ transplant can occur. The transplant, at this point, occurs in the same manner as any other organ transplant.

Once the transplanted uterus is shown to be functional, which is demonstrated by regular menstrual cycles, and the uterus has healed without complication (generally after a year), the saved embryos are transferred to the recipient just as with any other IVF procedure. If implantation is successful, the woman will become pregnant and gestate the child. The mother cannot endure a natural vaginal birth with the transplanted uterus; instead she is required to have a C-section. Generally after one or two births following a uterine transplant, the transplant doctor performs a hysterectomy to remove the transplanted uterus. This is intended to prevent complications that can occur from long-term use of immunosuppressants.

This breakdown of the process of UTx illustrates that although UTx is described as a single procedure, it is actually made up of several different procedures. We have already examined the risks and burdens associated with each step of this process, but it is important to note the cumulative risks of UTx. For a LD there are the physical and psychological risks and burdens of a hysterectomy as well as the psychological effects of an organ donation. For the recipient, there are the risks and burdens of egg harvesting, a hysterectomy, an organ transplantation, IVF implantation, pregnancy(ies), c-section(s), and a second hysterectomy. I do not enumerate these risks to say that UTx is *too* risky, I simply mean to emphasize that the risks and burdens are significantly greater that what one might expect from a single procedure.

One potential benefit of UTx is the experience of pregnancy, of gestating one's child. When a uterus is transplanted into the woman, the blood vessels are attached to the

transplanted uterus in order for it to gestate a child; however, the uterus is not innervated, because the nerves do not actually contribute to the organ's overall functioning (Castansos et al. 68). This means that a woman who is pregnant after UTx experiences the hormonal effects of pregnancy, such as morning sickness and fatigue. However, she will not experience other effects that require innervation, such as feeling fetal movements, and the feeling of contractions will not occur for a woman who has undergone UTx (Castansos et al. 68). While these sensations do not impede the achievement of the overall goal of UTx (i.e. gestating one's own child), they do factor into women's expectations of the procedure as well as their intention for going through the process. This distinctive pregnancy experience is a factor in discussion of the ethics of UTx for recipients, as will be seen later.

I do not mean to suggest that UTx is an overly risky surgery, nor do I mean to discredit the experience to potentially be gained from this advance. My hope in this background is to illustrate the gravity of the process. There is also a great deal of significance associated with the burdens of infertility, and UFI particularly, which is what makes discussion of UTx so important. When we examine the ethics of considering donors and recipients, this background will help demonstrate the caution with which UTx must be approached. However, I do not think that should discredit the hope that this procedure also offers. Caution and hope help to define the ethical considerations surrounding donors and recipients and eventually to determine the cases in which UTx is an appropriate treatment.

ASSESSING ETHICAL CRITERIA

As we have seen in looking at the procedures involved in UTx, a uterine transplant is, at its core, an organ donation being used as an ART. Because of this, the considerations and discussions surrounding organ donations and ARTs can provide helpful frameworks to examine UTx. It is important to note, however, that because UTx is *both* an organ donation and an ART, it is in and of itself distinct from both of these procedures individually, and therefore the discussion, justification, and objections will diverge slightly from both. In the next two chapters, the discussions of organ donations and ARTs inform an assessment of the current ethical criteria for *receiving* a UTx and the ethical criteria for *donating* one's uterus. The discussions of organ donations and ARTs also help in proposing and assessing potential addition criteria for both UTx candidates and donors in clinical practice. The final chapter examines lingering questions involved in the ethical clinical use of UTx such as allocation of uteri and payment for the procedure. The final chapter will also examine areas of UTx that require further research and discussion.

CHAPTER TWO: Ethical Criteria for UTx Recipients

INTRODUCTION

In countless articles about UTx, whether an in depth look at the procedure, a discussion of the findings, or an interview with researchers, the characteristic of UTx that stands out is the hope that it promises. Women with UFI have traditionally had no hope of becoming pregnant. While many turned to adoption or surrogacy to build their families, many others found those prospects insufficient. With UFI affecting approximately 15.4% of women of reproductive age in the United States in 2008, there are presumably many women grappling with the fact that they can never become pregnant (Nair et al. 83). Although still in the research phase, UTx gives these women an alternative to adoption or surrogacy that, to many, feels closer to a traditional reproductive narrative.

As with any medical treatment or procedure, however, UTx is probably not an appropriate treatment for every woman with UFI. The research teams have developed medical exclusion criteria to determine who are appropriate candidates to receive a uterine transplant, and while those criteria are exceedingly important, they cannot be the only guidelines for selecting a UTx recipient, especially when UTx becomes a part of clinical practice. There have been discussions regarding the ethics surrounding UTx and a beginning set of ethical criteria, but a robust set of guidelines has not been created to address the non-medical criteria for UTx in a clinical setting. In this chapter I examine the current ethical standards and discussions and expand upon them to begin establishing a more thorough set of criteria to determine whether an individual is an appropriate UTx candidate to receive based on non-medical factors.

CURRENT CRITERIA STANDARDS

The most robust set of guidelines that currently exists regarding UTx is the *Montreal Criteria for Ethical Feasibility of Uterine Transplantation*. Originally developed in 2011, this document lays out criteria, both medical and non-medical, that the recipient, the donor, and the health care team must meet in order for UTx to be appropriate in clinical use. These criteria assume that UTx will be "shown to lead to viable gestation and is proven to be medically safe for the mother and fetus" (Lefkowitz et al., "The Montreal Criteria" 444). The *Montreal Criteria for Ethical Feasibility of Uterine Transplantation* were updated in 2013 and are the criteria I examine throughout. The updated criteria are as follows:

1) The recipient
   a) is a genetic female of reproductive age with no medical contraindications to transplantation,
   b) has documented congenital or acquired UFI that has failed all current gold standard and conservative therapy,
   c) (c1) has a personal or legal contraindication to surrogacy and adoption measures and desires to have a child, or (c2) seeks the UTx solely as a measure to experience gestation, with an understanding of the limitations provided by the UTx in this respect,
   d) has not had her decision to undergo UTx deemed as irrational by expert psychological evaluation, and has no psychological comorbidity that interferes with diagnostic workup or treatment,
   e) does not exhibit frank unsuitability for motherhood,
   f) is likely to take antirejection medication and follow up with the treating team in a responsible manner, and
   g) is responsible enough to consent, informed enough to make a responsible decision.
2) The donor
   a) is a female of reproductive age with no medical contraindications to donation,
   b) (b1) has repeatedly attested to her conclusion of parity, or (b2) has signed an advance directive for postmortem organ donation,
   c) has no history of uterine damage or disease, and
   d) is responsible enough to consent, informed enough to make a responsible decision, and not under coercion.

3) The health care team
    a) is part of an institution that meets Moore's third criterion as it pertains to institutional stability,
    b) has provided adequate informed consent to both parties regarding risks, potential sequelae, and chances of success and failure,
    c) has no conflict of interest independently or with either party, and
    d) has the duty to preserve anonymity
    (Lefkowitz et al., "An Update of the Montreal Criteria" 924)

It is important to remember that this set of criteria is not binding, but is instead a recommendation. As research develops, the criteria will also have to be developed to incorporate any relevant findings. While these criteria represent robust and thoughtful ethical considerations, they bear expansion and further discussion of appropriateness.

In this chapter, I begin by examining the first set of criteria surrounding the recipient. One criterion to point out at the start is the requirement that the recipient is a genetic female. This suggested limitation denies the promise that UTx may provide for males or trans individuals hoping to gestate a child. Lefkowitz et al. point to several reasons why the criterion is necessary, at least at the moment. They point to the fact that animal and human trials have only dealt with genetic females to date; therefore, more research would be required in order to expand the recipient population. Additionally, they point to the other medical requirements to sustain a transplanted uterus in a non-genetic female, including "the creation of adequate uterine vascularization de novo, the necessity for appropriate hormone replacement to sustain implantation and pregnancy, and the placement of the uterus in a nongynecoid pelvis" (Lefkowitz et al., "An Update of the Montreal Criteria" 924). These requirements make the surgery more complicated and have been subject to very little research. For these same reasons, the discussion here surrounding the ethical considerations of recipients of UTx will pertain only to genetic females. As Lefkowitz et al. discuss, this is not to say that it is unethical for a non-genetic

female to receive a uterine transplant; we simply need further research into the medical feasibility of this before changing this criterion. This issue is discussed in chapter four as I look at future research considerations. However, for the time being, I assume that this criterion is legitimate; therefore the remainder of the discussion in this chapter will assumes that the only recipients of UTx are genetic females.

RELEVANT ETHICAL CONCEPTS

Just as the frameworks and discussion surrounding organ donations and ARTs influence our discussion of UTx, there are several ethical concepts that influence the development of a set of criteria. As I address several of the main ethical discussions regarding recipients of UTx, it is important to consider these ethical principles. In the first chapter, I discussed the principles of beneficence and nonmaleficence, two principles that will inform any requirements for UTx to be considered ethical. Beneficence is the obligation or duty to promote the good, while nonmaleficence is the obligation or duty to not inflict harm (Beachamp and Childress).

Beauchamp and Childress also focus on the principles of justice and autonomy. Like to beneficence and nonmaleficence, both of these principles are relevant to the discussion of requirements for a UTx recipient. Justice, which is touched on later in discussing organ allocation, is a principle of fairness and equity (Beauchamp and Childress 241). Autonomy, and more specifically respect for autonomy, is the principle that individuals have the right to make decisions for themselves, which doctors have an obligation to honor (Beauchamp and Childress 99, 103). Beauchamp and Childress stipulate that in order to respect an individual's autonomy, that individual must be found

to be able to competently make a decision and must be adequately informed about the decision (Beauchamp and Childress 117-121). It is important that all four are *prima facie* principles, meaning they are to be upheld unless they contradict or are in tension with one another under the circumstances. For example, sometimes avoiding harm (nonmaleficence) may fly in the face of autonomy, and in some cases it can then override the obligation to protect autonomy (Beauchamp and Childress 14-16).

Another ethical concept that is relevant in establishing ethical requirements for UTx is the risk-benefit ratio. This concept entails determining the risks of harm in a given situation, determining the potential benefits of a given situation, and weighing these against one another to determine the best course of action. This is perhaps the most prominent concept I use in this discussion as I address what are acceptable risks and whether they are reasonable in relation to anticipated benefits. The weighing of risks and benefits is a subjective process. Some benefits may seem strong for one individual, but trivial to another. When utilizing this concept, therefore, it is important to consider the risks and benefits as viewed by the most relevant parties, which in the case of UTx are the recipients and the donors.

These ethical principles and concepts are not an exhaustive list of all of the ethical concepts at play. However, they are several of the main concepts that inform the ethical criteria and discussions of organ donations and ARTs. For this reason, they are particularly relevant when determining a set of criteria for the ethical use of UTx in general, and particularly in this chapter, ethical considerations for a UTx recipient.

RECIPIENT'S EXPERIENCE

As discussed in the first chapter, this procedure is much more extensive than a single surgery. For the recipient, UTx involves ovarian stimulation and subsequent egg harvest, a hysterectomy (if she has a non-functional uterus in her body), an organ transplant, IVF (occurring both before and after the transplant), 1-2 pregnancies followed by C-sections, and a hysterectomy. The extensive nature of this multi-step procedure makes UTx fairly cumbersome and risky. This aspect of UTx affects the risk-benefit ratio of the procedure, which, affects whether or not a potential recipient is an appropriate candidate for the procedure.

Another fundamental aspect of UTx is the distinction between the ultimate goal of UTx and what the procedure medically accomplishes. The goal of pursuing UTx is to have a baby, specifically to be able to gestate a baby. Although this outcome is the ultimate goal of UTx, a medically successful procedure cannot guarantee it. While early human uterine transplants were considered "successful" because the organ was transplanted successfully and gained function as determined by menstruation, they did not result in the recipient giving birth to a baby (Fageeh et al. 245-251; Brännström et al. 610-613). Because of this, it seems impossible to believe that the recipients of the transplant viewed their surgery as successful. I point this out to illustrate that, just as with many medical procedures, the potential benefits and the desired ultimate outcome of UTx are not guaranteed. Therefore, when the concept of the risk-benefit ratio is applied to assess and determine ethical criteria for a UTx recipient, the uncertainty of achieving the desired outcome, even with a medically successful surgery, must be taken into account.

In the rest of this chapter, I examine various ethical criteria specific to UTx recipients. The following chapter takes a similar approach in examining ethical criteria for UTx donors. The criteria addressed are not exhaustive, nor are they binding. This discussion is meant to elucidate and expand upon current ethical criteria and expand upon those to determine a more robust set of criteria for the clinical use of UTx. As UTx moves from the realm of research to treatment, there are many more criteria that will need to be considered. The following, however, seem to be the most likely ones that clinicians will face when determining whether to proceed with this procedure in any given case.

ETHICAL ASSESSMENT OF CRITERIA FOR UTX RECIPIENTS

The remainder of this chapter provides an ethical assessment of criteria for UTx recipients, both existing criteria and possible additional criteria. While some of these considerations are currently included in The Montreal Criteria, others are not. Both existing criteria and any proposed additions are assessed according to the ethical principles and concepts outlined above to determine whether they should be included as formal criteria for a recipient of UTx in the clinical setting.

REASON FOR PURSUING

As stated, there are a number of women for whom UTx could serve as an infertility treatment. Among women with UFI, there is presumably a large group that does not wish to seek UTx. Perhaps they do not wish to have more children, or to have

children at all. Or maybe they feel comfortable pursuing surrogacy or adoption to create or grow their family. But the remaining group that would seek UTx as an option to treat their UFI, may have many different reasons for pursuing UTx. For example, some women may pursue UTx because for moral or legal reasons they cannot pursue adoption or surrogacy, while other women may wish to gestate their child; still other women may see UTx as a chance to experience a more "normal" path to parenthood, and others may feel incomplete given their condition and see UTx as an opportunity to restore their body to "normal".

The question then becomes why particular reasons matter. If a woman desires to receive UTx for *any* reason, should she be able to receive the transplant, as long as she has met all other criteria. The Montreal Criteria speaks to the woman's reason in point 1c, stating that she must either "[have] a personal or legal contraindication to surrogacy and adoption measures, or [seek] the UTx solely as a measure to experience gestation, with an understanding of the limitations provided by the UTx in this respect" (Lefkowitz et al., "An Update of the Montreal Criteria" 924). In this section I look at three categories of reasons for pursuing UTx and assess the ethical permissibility of each. The first category is one that the Montreal Criteria pointed to, which is women who wish to experience gestation; the second category is women who see UTx as a chance to restore bodily integrity; and the third category is women for whom UTx is the only viable option for becoming a mother for moral or legal reasons.

To Experience Pregnancy

The first reason for pursuing UTx that I address is the desire to experience

pregnancy. In criterion 1c of The Montreal Criteria, " [seeking] the UTx solely as a measure to experience gestation, with an understanding of the limitations provided by the UTx in this respect" is deemed an acceptable reason to pursue UTx (Lefkowitz et al., "An Update of the Montreal Criteria" 924). However, among women who cite their reason for pursuing UTx as a chance to "experience gestation," their concept of what this experience is may differ. Some women may desperately want to go through gestation because it is an experience that is "universal" among women and they desire to relate to other women's pregnancy and birth narratives. Other women may feel shame regarding their infertility and see experiencing gestation through UTx as a chance to make them more "normal." Still other women may want to experience gestation to achieve closeness to their child through the nine months of pregnancy. Because the understanding of what it is to "experience gestation" and the reasons behind this desire are so expansive, the Montreal Criteria's approval of UTx for a woman wants to "experience gestation" (as long as she is properly informed of what that means) feels too glib.

As the universality and shame narratives both point to, infertility and pregnancy are deeply tied to a woman's identity (Czarnecki 717). In a review of the literature on psychological effects of infertility, several themes emerged including: infertility as a central focus for identity, feelings of defectiveness and reduced competence, feelings of alienation from the "fertile world", and a sense of social stigma (Greil1682). Several of these effects could perhaps be more effectively combatted by UTx than by other alternative reproductive measures. For example, while surrogacy can help a woman or couple build a family, it still probably leaves a woman with a feeling of defectiveness, making her feel as though she is incapable of doing something that her surrogate can do.

With UTx, on the other hand, the woman hopes to become pregnant. Furthermore, by actually gestating her child, she is then able to participate in the camaraderie that comes with pregnancy, even though her pregnancy is different from a traditional pregnancy. In addition to these psychological effects, studies have shown that on the whole women who face infertility have twice the prevalence of depressive symptoms relative to fertile women (Cousineau and Domar 295). A woman's desire to experience pregnancy does not exist in a vacuum, but rather is influenced by societal pressures and norms, which result in very real and devastating mental effects for women who experience infertility. We must consider the pressure any given society puts on women to bear children and the degree to which pronatalism affects a society, and specifically its women. This does not mean that the acceptable reasons for a woman pursuing UTx will differ society-to-society; but when a woman's reason for pursuing UTx and her ability to understand its risks and benefits are assessed, the effect of her society, whether country, religious group, or socioeconomic group, must be examined. In the United States, pronatalism "[glorifies] procreation and childbirth, while at the same time stigmatizing infertility and adoption" (Bartholet 9). Does this then mean that we should allow women to fulfill their desires to experience pregnancy to avoid the stigmatization of infertility? Or does this reasoning further the stigmatization of infertility, surrogacy, and adoption and, if so, should we resist it?

One consideration when a woman states that she wants to pursue UTx to experience pregnancy is the issue of informed consent. Informed consent is a requirement that is unique neither to UTx in general nor to assessing a woman's reason for pursuing UTx. There are, however, important aspects of understanding a woman's reason for

pursuing UTx that a clinician must be aware of when assessing a woman's informed consent in this area, which in turn will determine if a woman is an appropriate candidate for UTx. Women pursuing UTx probably have a specific idea of pregnancy in mind that they expect to count as part of their own childbirth narrative. For some, pregnancy is associated with morning sickness, for others it may be swollen feet and back pain, others may look forward to the first time they feel the baby kick, and still others may look forward to trying for a natural birthing process. For women who have undergone UTx, their pregnancy experience may deviate from their previous expectations. As mentioned in the first chapter, because the transplanted uterus is not innervated, a UTx recipient will not experience some of the effects of pregnancy that require nerve endings, such as feeling the baby move. Furthermore, the requirement of a C-section makes a woman's birth story different from what she may desire. If it is acceptable for a woman to pursue UTx due to a desire to experience pregnancy, medical providers must understand what exactly a woman means by "experiencing pregnancy." Even if a desire to experience pregnancy is an acceptable reason for pursuing UTx, as the Montreal Criteria suggest, if a potential UTx recipient misunderstands what a pregnancy brought about by UTx misunderstands what UTx can actually accomplish, it is unethical for a provider to consider her as an acceptable recipient of UTx. If, for example, a woman seeks UTx to "experience gestation," which to her means experiencing everything associated with a "typical" pregnancy, and if this understanding persists after her medical team seeks to educate her about the limitations and experience of UTx, then she is not an acceptable UTx recipient.

Moral or Legal Contraindications

This reason for pursuing UTx may seem like it does not bear much discussion. It was largely with this category of women in mind that the procedure was developed. But even within this straightforward reason, it is unclear what exactly counts as a personal or legal contraindication. A legal reason for some may just be that surrogacy laws are complex, and the possibility of disagreement between the parties makes the outcome uncertain, which may understandably make the potential parents wary of pursuing this as an option. Does this nervousness count as a true legal contraindication as the Montreal Criteria require? Whether the answer is yes or no, I think the question remains: How strongly must a woman find herself in personal or legal opposition to surrogacy or adoption in order to establish that it counts as a contraindication, so that she may pursue UTx?

A follow up question to understanding what counts as a contraindication is: What is the burden of proof of these contraindications? Does a woman need to bring a note from her religious leader, much like a child brings in a doctor's note to get out of school activities? Or is it enough for a woman to explain to her medical team why neither surrogacy nor adoption is a viable option for her? If we place too great an emphasis on requiring a moral or legal contraindication, I worry that this will be inconsistently assessed from doctor to doctor.

Even though this reason is in a sense the most straightforward, some might challenge even this reason for pursuing UTx. It is feasible that someone might view infertility as a woman's lot in life and argue that if she chooses not to pursue surrogacy or adoption, even because of moral or legal contraindications, then she must accept not

becoming a mother because the risks and cost associated with UTx are not outweighed by her reasons. This argument is lackluster because it ignores the fact that the same could be said of many procedures. For example, one could say simply say that if a woman or couple does not wish to adopt then they are choosing not to become parents, because the cost and risks of surrogacy are too high. Because this argument is not evenly applied in medicine or even in assisted reproduction, it falls short.

If the desire to experience gestation through UTx, as long as adequately understood, is an acceptable reason for pursuing UTx, then why include a criterion for a contraindication of any sort? I think that a clearer criterion regarding an acceptable reason for pursuing UTx, to replace 1c of The Montreal Criteria, would be as follows: the recipient seeks the UTx with the goal of having a child and the desire of experiencing gestation, as well as an adequate understanding of the limitations provided by the UTx in this respect. As seen in the next subsection, it would be too expansive to allow a recipient to receive a UTx for any reason. Furthermore, I believe that the goal of *having* a child, in addition to gestating a child, needs to be added to the criterion. Although it seems a story of science fiction, it is not terribly hard to imagine a woman with UFI seeking a UTx in order to experience gestation, but having no desire to be a mother, and thus seeking to act as a surrogate for others or choosing to give the child up for adoption. It is far-fetched, but bears discussion. A scenario like this would be unacceptable for two reasons. The first is that it ignores the ultimate goal of UTx, which is to have (i.e. parent) a child in addition to simply gestating a child. The second reason this scenario is unacceptable is that it changes the risk-benefit ratio of the procedure. Without the benefit of becoming a parent via UTx, the risks of the procedure and use of immunosuppressants become

weightier.

Bodily Integrity

One category of a reason for pursuing UTx that The Montreal Criteria do not address is the desire to restore bodily integrity. More than other types of infertility, UFI affects a woman's concept of her bodily integrity. As the psychological effects suggest, a uterus is a key part of a woman's feminine identity. As mentioned, infertility is often accompanied by feelings of defectiveness that affect a woman's identity. The question then arises, what if a woman wants to pursue UTx, not to become pregnant, but to restore her feminine identity and bodily integrity?

In the Montreal Criteria expansion, Lefkowitz et al. suggest that that if a potential recipient has no desire to carry a child, the procedure cannot be justified (Lefkowitz et al., "An Update of the Montreal Criteria" 925). There are perhaps a couple of reasons for this assessment. The first reason is that this is not in line with the purpose of the procedure (Bayefsky & Berkman 354). The actual purpose of the procedure is to enable a woman to gestate a child. The Montreal Criteria even states that if a woman's goal is simply to have a child, without the added desire of carrying a child, UTx is not an appropriate procedure, but rather she should pursue adoption or surrogacy, which would still achieve her goal (Lefkowitz et al., "The Montreal Criteria" 445).

Another reason that bodily integrity cannot justify UTx is because it changes the nature of the procedure itself. Presumably if a woman wishes to restore bodily integrity, the subsequent hysterectomy that accompanies UTx would not occur. Leaving the uterus in place requires long-term immunosuppression, increasing the risk of UTx for the

recipient. One might argue that certain transplants, such as face transplants, have a goal of restoring bodily integrity and helping the recipient's sense of identity. Even if the effect of a UTx on identity is the same as that of a face transplant, a uterus itself affects one's daily life less significantly than one's face. Therefore, even though there are legitimate and serious psychological effects, the benefits garnered from surgery are different. For these reasons, the risks of UTx and the prolonged use of immunosuppressants are not reasonable in relation to the benefits. Therefore, UTx for the reason of restoring bodily integrity is not ethically acceptable. If the risks of long-term immunosuppression could be reduced, it may become acceptable to use UTx to restore bodily integrity. At that point, the potential benefits would still need to be weighed against the risks of surgery, but given the other cases in which we use transplants to restore bodily integrity (e.g. face, limb, and hand transplants), it is likely that it would be deemed acceptable. Another discussion that would, at that point, be necessary is whether a woman's goal of UTx (have a child vs. restore bodily integrity) would affect allocation of uteri for transplants.

For each of these reasons for pursuing UTx, the heart of the issue is the risk-benefit ratio. Given that the surgery carries many risks of harm, the potential benefits must be deemed greater than the risks involved. It is for this reason that certain reasons for pursuing UTx are acceptable, while others, such as bodily integrity, do not provide enough potential benefit over one's current state to justify the potential risks. One question that this raises, however, is who is to determine whether any, however miniscule, potential benefit is greater than the risk? Does this burden of judgment fall on

individual doctors? Does it fall on a governing board or association to determine generalized rules? Or is an individual patient capable of weighing these risks and benefits for herself?

MOTHERHOOD STATUS

One criterion that is absent from current ethical criteria for UTx is a recipient's current motherhood status. Although this is not addressed in any formal criteria, it is addressed in discussions of UTx and infertility in general, and therefore must be addressed when assessing and establishing criteria for the ethical use of UTx. For some women, UFI is acquired rather than congenital, which means that some women suffering from UFI have already been pregnant and given birth to biological children. Is UTx an appropriate treatment for these women, as well as for those who have never experienced pregnancy and childbirth?

One argument against UTx as an acceptable option for mothers with UFI is that they have already had the opportunity to experience what women with UFI and other types of infertility are seeking (Del Priore and Gudipudi 21). Del Priore and Gudipudi extend this argument not just to women who have carried a biological child, but to those who have previously pursued and had a child through either surrogacy or adoption, citing that they do not have a need to take on the risks of UTx. This argument is problematic for several reasons. Although UTx carries risks which, when compared to its potential benefits, can render it an unacceptable practice in some cases, this argument is paternalistic in that it deems some women unable to weigh these risks against their particular potential benefits. It also ignores the fact that some women who have had at

least one biological child desire to have additional genetically related children they have gestated.

Furthermore, Del Priore and Gudipudi's attitude toward motherhood status indicates the ways in which the medical community and literature view infertility as a physiological state rather than as a psychosocial status (Greil 1694). By disqualifying mothers from pursuing UTx, they are saying that the end goal of having a family is the only relevant goal. In one set of accounts in which women with infertility (not limited to UFI) were interviewed about their experience, one mother said this:

> Having two children has not taken away my infertility. It is still with me and so are the feelings of resentment and anger, sadness, et cetera, that go with it. The joy that I get from my family fills my thoughts most of the time. People ask me if I'm going to have any more children, and negative feelings arise because I resent that I don't have that 'easy' choice as others do. [Egg recipient (known donor), potential embryo donor, Australia] (Kirkman 244)

As this woman stated, infertility becomes about much more than just having a child. It becomes an identity and a psychosocial status. This self-perceived status does not dissipate just because a woman already has had a child or because she has used a surrogate or pursued adoption. Given the lasting effects of this psychosocial identity, a woman who has already had children should be not be viewed differently from a woman without children when both pursue fertility treatments.

If it is acceptable to pursue UTx to experience gestation, as discussed in the previous section, then that criterion should not be applied differently depending on

whether a woman has a previous child, whether genetically related to her or not. In stating that a current mother should not be allowed to pursue UTx, nonmaleficence is being applied differently to her than to a woman without children. If in applying the principles of nonmaleficence and beneficence to a woman without children who seeks to pursue UTx, it is deemed an acceptable procedure, then that same result should apply to a woman with children, all other things being equal. By upholding that woman's autonomy, we allow her to assess the risk-benefit ratio for herself. Some women who already have children will view the risks of surgery as outweighing the potential benefits, and therefore may choose to view their family as complete. Other women may see an immense potential benefit from growing their family and thus still may be potential recipients of UTx.

Although a woman's motherhood status should not affect the permissibility of UTx, it is feasible and perhaps acceptable that it should affect organ allocation. This is touched on in the final chapter, but it is important to hold issues of ethical allocation separate from issues of ethical acceptability of UTx recipients.

AGE

Another ethical consideration with regard to whether a woman is an appropriate UTx recipient is age. There are two reasons for which age must be considered. The first aspect is any additional medical considerations surrounding age, and the second aspect is whether age affects a woman's ability to parent. The determination of the medical component of this criterion must fall on the physician, because advanced maternal age does bring more potential medical complications. Pregnancies in women of advanced

maternal age carry greater risk of chromosomal abnormalities in the child as well as greater risks to the mother (Heffner 1928). These medical assessments and risks are conversations to be held and decided on between the physician and patient. Given the differences in each patient, these decisions will probably have to be made on a case-by-case basis in order to ensure the safest possible scenario for mother and child. Although advanced maternal age carries additional risk in pregnancies, this aspect alone does not render UTx unacceptable in all cases with recipients of advanced maternal age. As long as the risk-benefit ratio is acceptable generally, then whether the risk-benefit ratio is acceptable for a particular recipient is based on her informed decision according to the principle of respect for autonomy.

One important factor to note with regard to the medical aspect of UTx and maternal age is that, for the time being, UTx is restricted to use with the recipient's own eggs. If a woman has already undergone menopause, and has not previously frozen her eggs, UTx is not an option for her. We will discuss this in the final chapter as we look at the future of UTx and the potential expansion of the pool of recipients, however for the time being, this still is a hard and fast upper limit on age of a recipient as determined by her oocytes.

The second facet of maternal age and UTx is a more social factor, which is whether maternal age affects a woman's ability to parent. The concept of a woman's ability to parent is addressed in the next section, but given the other factors surrounding maternal age, I touch on how age factors into this here. While the medical component only considers *advanced* maternal age, this social aspect could play a role in a potential mother's being deemed too young or too old. There is no data stating that age (either too

old or too young) indicates an individual's parenting ability; thus it is impermissible and discriminatory for age, as it pertains to one's ability to parent, to be used as a criterion for whether or not a woman is an appropriate recipient of UTx.

As mentioned within the context of motherhood status, one final aspect of the ethical considerations surrounding a potential recipient's age is how age should affect uterus allocation. In the final chapter, I look at uterus allocation, but it bears particular mention here given the role age plays in this discussion. In all organ donations, age is a prominent factor when determining who is to receive an organ first, but the way in which age plays a role varies depending on the organ in question (Bayefsky and Berkman 355). For some transplants, a score is used to compare recipients. In some cases, the scoring places a high value on the graft longevity and maximizing the use of the organ (Bayefsky and Berkman 355). Other times, however, age factors less into a patient's score than the urgency of his or her need (Bayefsky and Berkman 355).

The two arguments that are made when discussing age and organ allocation are the fair-innings argument and the prudent lifespan account. A fair innings argument prioritizes younger patients by stating that every individual is entitled to their fair share of life experiences (Bayefsky and Berkman 355-356). Norman Daniels' prudent lifespan account similarly tends to favor allocation toward younger patients; however, it does so by encouraging society to come to a consensus on how to allocate resources across a single lifespan (Daniels, Just Health). The prudential lifespan is intended to work against pitting age groups against one another in the allocation battle, by also examining how long the organ will be used. If a younger patient receives a high quality organ and can get more years of use out of it than an older patient can, then the argument states thatgiving

the organ to the younger patient is a better use of the scarce resource; therefore, choosing the younger patient is the prudent decision (Bayefsky and Berkman 356-357).

Applying both of these arguments to UTx, it seems that recipients who fall within normal childbearing years will be prioritized. As Bayefsky and Berkman point out, the fair innings argument would, however, prioritize those women nearing the end of their childbearing years ahead of those women at the beginning of that stage. One question that this argument raises, however, is what is normal childbearing age? The World Health Organization defines normal childbearing age as being 15-49; however, a woman's ability to conceive can extend past that on both sides (Bayefsky and Berkman 357). Given the subjective nature of this decision, this is an area in which the governing medical organizations need to reach consensus and issue a recommendation rather than allowing doctors to determine for themselves.

SUITABILITY FOR MOTHERHOOD

A woman's suitability as a mother, and the factors that go into this judgment, is a discussion that is prevalent in discussions of ARTs. Where most considerations for organ donation recipients focus on whether an individual is a good candidate medically (with the exception of discussions of adherence, which I address later), ARTs, as is the case with UTx as an ART, must focus on the final hopeful outcome, which is parenthood rather than merely having a new organ. Because of this difference in the ultimate goal of the procedure, it is appropriate and even necessary to consider a recipient's ability to parent. That being said, there are certain considerations that are appropriate and relevant and others that are not. Below I touch on several of these considerations to elucidate what

factors doctors should consider and which are not acceptable bases on which to make a decision. All of these categories involve weighing the reproductive interests of the individual (potential recipient) against the welfare of the future child and the professional autonomy of the provider.

Relationship Status & Sexual Orientation

Defining parenting is key to understanding how relationship status and sexual orientation do or do not fit into an individual's or couple's ability to parent, and therefore a woman's or couple's acceptability as a UTx recipient. In order to address this, we must ask the question: Is having two individuals, one of each sex, essential to the act of parenting?

This question is not particular to UTx, or even ARTs in general; it also comes into play when considering adoptive families. Currently, all states allow gay and lesbian couples as well as single people to foster children, and most states allow all of these categories of people to adopt (ASRM, 1525). That being said, adoption regulations prioritize families that mirror the traditional ideal of a family: two parents, a man and a woman, who have demonstrated marital stability (Bartholet 8). This reality flies in the face of what is technically set forth in the law. Although this prioritization is different from prohibiting gay and lesbian couples from adopting, it is unethical unless there are acceptable data that supports the a claim that a traditional adoptive family is better for the welfare of the child than a non-traditional adoptive family. However, there are no data supporting this prioritization.

Certain countries, such as France, have restricted ART use, which would include

UTx if and when it becomes a treatment, to heterosexual couples only (Berekfsy and Berkman 360). The American Society for Reproductive Medicine (ASRM), however, rejects this stance on the basis of equal treatment and lack of data. They have said that there are no data to support the claim that parental sexual orientation or relationship affects a couple's ability to parent; therefore, the welfare of the future child is not being harmed. Given that there are no data to indicate that homosexual couples or single individuals are lesser parents, the argument against allowing these individuals or couples to pursue parenthood is simply based on a provider's moral objection. ASRM also stated that "moral objection to homosexuality or single parenthood is not itself an acceptable basis for limiting childrearing or reproduction" (ASRM, 1525). They further emphasized this stance by saying that "as a matter of ethics, this Committee believes that the ethical duty to treat persons with equal respect requires that fertility programs treat single persons and gay and lesbian couples equally to heterosexual married couples in determining which services to provide" (ASRM, 1526).

The ASRM's recommendation makes this ethical consideration of a UTx recipient very clear. If a lesbian couple or single woman seeks UTx, a doctor's moral stance against homosexuality or homosexual parenting should not permit him or her to prevent the individual or couple in question from pursuing UTx.

Child Rearing Capacity

As mentioned, a factor differentiating UTx from other organ donations is that its goal is not just to complete a successful transplant, but to achieve parenthood. Because of this ultimate goal, an individual's or couple's child-rearing capacity has to be considered

(Bayefsky and Berkman 359). We have already addressed arguments that try to confer meaning upon age, relationship status, and sexual orientation as indicators of this capacity. Although those indicators have been dismissed as factors in and of themselves, there are other ways to determine whether individuals or couples are acceptable parents and therefore whether they are appropriate candidates for UTx.

One argument against assessing this capacity is that if a woman were to get pregnant naturally, no one would assess whether she is able to raise a child. Is it then acceptable to hold women who cannot get pregnant naturally to a higher standard (Gurmankin et al. 61-62)? This argument has been addressed with all other forms of ARTs that have come before UTx, and the general conclusion is that yes, it is acceptable to implement more rigorous requirements for women and couples pursuing alternative reproductive methods. The reason this screening is acceptable is because of a societal interest in the future welfare of the child (Gurmankin et al. 64-65). Even though the recipient of the UTx (or any other ART) is the patient, the medical provider still has a responsibility toward the future child; therefore, it is acceptable and even necessary to assess a woman's or couple's suitability as parent(s).

As already mentioned, potential adoptive individuals and couples are assessed for suitability. Some states require criminal background checks, while others require child abuse background checks (Bayefsky and Berkman 359). Still others require that parents prove that they have the financial means to raise a child (Bayefsky and Berkman 359). Some would argue, however, that UTx is unlike adoption, in that it is a medical treatment rather than a social service, and requirements like these cannot be imposed on a medical treatment (Bayefsky and Berkmen 359-360). Although UTx addresses infertility in a

more medicalized manner than adoption does, the aforementioned goal of UTx means that the social aspect cannot be divorced from the medical. Therefore, the precedents set forth in adoption and even ART restrictions can be applied and adapted to potential UTx recipients.

Bayefsky and Berkman advocate for requiring a minimum child-rearing capactity standard, similar to what the ASRM has recommended for other ARTs (Bayefsky and Berkmen 359). In practice this would mean that potential recipients are not ranked or scored against one another; they simply would have to be able to prove several factors about their capacity to parent. One way in which this minimum standard is distinct from a ranking is that it cannot be used as a means of allocation according to who would be the best parents. As long as individuals or couples have proven that they meet the standards, they cannot be said to be more or less worthy of a uterus than any other individual or couple that has met the same standards.

Similar to the common standards set forth in adoption restrictions, potential recipients (and the other parenting partner, if relevant) should be required to pass both a criminal background check and a child abuse background check. The minimum standard should also include a financial assessment, not to favor wealthier individuals or families, but to ensure a minimum level of wealth. Each of these standards prioritizes the future welfare of the child over the reproductive interests of the parent(s) and ensures that the doctor or state is not acting negligently (Bayefsky and Berkman 360).

The burden of ensuring these requirements should fall on both the state, as it does with adoption, and the medical teams interacting with the UTx candidates. In order to protect the welfare of the future child, the state must set these standards by law to

guarantee that they are upheld. When a medical team is presented with a potential recipient, the team then has the burden of ensuring that the standards set forth by law are in fact met before proceeding. On the flip side, having these minimum standards also means that a doctor cannot arbitrarily decide that individuals or couples are unfit parents by appealing to considerations outside of these criteria.

ADHERENCE

The final ethical consideration for recipients is adherence. As discussed previously, the transplant itself is a part of a set of procedures that together are aimed at the birth of a child. The set of procedures as a whole requires consistency in medication and medical follow-up. The revised Montreal Criteria states that in order for UTx to be permissible, the potential recipient must be "likely to take antirejection medication and follow up with the treating team in a responsible manner" (Lefkowitz et al., "An Update of the Montreal Criteria" 924). Precedents set in organ transplants and gender reassignment surgery justify a requirement to prove adherence.

As briefly mentioned in the introduction of this section, most requirements for determining whether an individual is a good candidate to receive an organ donation revolve are medical factors: are they a good match? are they an acceptable age? etc.. Adherence is one factor that lies outside the black and white medical standards. In order for individuals to be appropriate organ recipients, they must demonstrate that they are able to take care of the organ after transplant, thus ensuring that the most benefit is achieved from the organ. For example, alcoholics can be precluded from receiving an organ donation if they cannot demonstrate that they can adhere to the medical

requirements after surgery (i.e. not drinking alcohol)(Lefkowitz et al. 446). Organ recipients also must demonstrate their ability to maintain their treatment plan by regularly taking immunosuppressants to prevent the organ from being rejected. Similarly, patients with gender dysphoria must demonstrate consistent and compliant use of hormone treatments for one full year before genital sex reassignment surgery can be offered (Lefkowitz et al. 925).

Both of these precedents indicate that a potential recipient must somehow demonstrate that they will be adherent in two ways: 1) that they will consistently take their immunosuppressant therapy as prescribed and 2) that after 1-2 live births, they will undergo a hysterectomy to remove the transplanted organ, a requirement that is unlike that applied to any other Tx. It is difficult to determine exactly how these two things can be demonstrated. In addition to being difficult to assess in general, transplantation literature describes a fear that assessments of potential adherence may disproportionately affect certain racial groups or individuals of lower socioeconomic status (Lockwood et al.). Finding an ethical way to assess the potential adherence of UTx recipients is something that the governing bodies, such as the ASRM, need to consider. Perhaps just as the Endocrine Society created guidelines for providers and patients with gender dysphoria, the ASRM needs to create a yearlong procedure and process by which potential recipients can prove themselves to be adherent prior to surgery. The determination of adherence cannot be left solely to a provider's determination; rather, there needs to be an overarching standard by which providers can assess their patients.

As UTx moves from research to treatment, it is also important to consider what will happen if a patient does not adhere. If a patient is non-compliant in taking her

immunosuppressants, there are clear medical consequences that will need to be addressed. More interesting, and perhaps concerning, is the potential that a patient will not consent to having the transplanted uterus removed after 1-2 live births. How is the medical community to address this issue? The answer is certainly not that the organ be forcibly removed, an option that ignores the principles of respect for autonomy and nonmaleficence. Nor is the answer to cease filling the patient's immunosuppressant prescription, which would similarly ignore the principle of beneficence. Does the medical team have any power or ability to enforce this last aspect of the total procedure then? This is a question that will remain, but certainly must be discussed and addressed as UTx moves closer to being a treatment option.

CONCLUSION

This ethical assessment of criteria that are or might be used to evaluate whether an individual is a suitabile recipient of UTx is far from exhaustive. There are certainly many factors that I did not discuss, and even more certainly, there are many considerations that will be brought to light the further UTx moves in research and the more it is eventually used as a treatment option.

One category I did not discuss in this chapter is a recipient's ability to pay for UTx, which is more accurately a recipient's ability to pay for the many procedures that make up UTx. This was intentionally left out for the time being, because, as we will see, it is a discussion that extends far beyond UTx itself. I briefly take up the discussion of insurance and a recipient's ability to pay in the final chapter as I discuss the future of UTx.

I have looked at each each of these criteria independently of one another. This is not a luxury that a medical team gets in real life. In a real life scenario, as with any treatment, all of these factors are at play to different degrees. Medical boards and individual medical teams must take great care to ensure that all potential recipients are being treated equitably, while also allowing room to determine permissibility on a case-by-case basis.

CHAPTER THREE: Ethical Criteria for UTx Donors

INTRODUCTION

At present, UTx trials have used all of the various types of donors: living, deceased, altruistic, related, and unrelated. As in any trial, selection criteria for each of these are laid out their from the start. Selection criteria applied to the donated uterus or the donor herself are medical criteria to ensure that the uterus is not damaged and has a reasonable chance of achieving pregnancy. Beyond the medical criteria, however, the inclusion criteria for donors can vary from trial to trial. While there has been much discussion of ethics as applied to selecting donors, especially regarding the use of living versus deceased donors, there is a lack of consensus about the ethical standards by which to determine what is an appropriate type of donor and how to assess individual donors. This chapter addresses the ethical selection of UTx donors in clinical use by assessing the current criteria for UTx donors, suggesting additional ethical criteria for UTx donors that should be considered, and discussing some of the major ethical dilemmas surrounding UTx donors.

CURRENT CRITERIA STANDARDS

As discussed in Chapter 2, the most robust set of ethical criteria regarding UTx is the *Montreal Criteria for Ethical Feasibility of Uterine Transplantation.* Below is the second section of the criteria, discussing the criteria for an appropriate UTx donor. The donor criteria as laid out in the 2013 revision of the Montreal Criteria are as follows:

4) The donor

a) is a female of reproductive age with no medical contraindications to donation,
b) (b1) has repeatedly attested to her conclusion of parity, or (b2) has signed an advance directive for postmortem organ donation,
c) has no history of uterine damage or disease, and
d) is responsible enough to consent, informed enough to make a responsible decision, and not under coercion.

(Lefkowitz et al., "An Update of the Montreal Criteria" 924)

These criteria touch on some of the biggest arguments regarding UTx donation, yet ithey are non-binding nor exhaustive in discussing all of the relevant ethical issues. Furthermore, and perhaps most notably, The Montreal Criteria does not address the possibility of using deceased donors. I use these criteria as a starting point to unpack several of the major ethical considerations applied to UTx and propose potential additions for the selection of UTx donors in clinical use.

RELEVANT ETHICAL CONCEPTS

Many of the ethical concepts relevant to UTx donors in clinical use are the same as those relevant to UTx recipients. Those that I discuss are beneficence, nonmaleficence, justice, autonomy, and risk-benefit ratio. Although the concepts are the same, applying them to the donor, rather than the recipient, can be rather different. The concepts of justice and autonomy apply in a very similar manner, but beneficence, the obligation of a clinician to promote the patient's good, and nonmaleficence, the obligation to avoid harm, are very different when you consider that the donation is promoting the good of an individual other than the donor and the procedure, by its nature, carries risk and has the

potential to harm the donor. These concepts and their application are largely similar to how they would be applied to any discussion of an organ donor.

The general concept of the risk-benefit ratio is the same. It requires one to determine the risks of harm as well as the potential benefits and weigh them against one another. The difference in the case of organ donors is that we must look at the *aggregate* risk-benefit ratio. If we just look at the risks and benefits to the donor, it is apparent that the risks will probably outweigh the benefits because the donor receives no physical benefits herself. The aggregate risk-benefit ratio, on the other hand, allows for risk to be taken on by one individual and weighed against the potential benefit to another individual. This concept is one that is used in organ transplants in general, as well as in research. Although the aggregate risk-benefit ratio allows risk to be taken on by the donor, it is important to remember that nonmaleficence is not disregarded; therefore, even if the overall benefit to another individual is great, the risks taken on by the donor still must be minimized.

DONOR'S EXPERIENCE

As mentioned, one of the main ethical issues is the appropriateness of using an LD. I spend a great deal of time discussing this in the next section of this chapter, but at the outset, I examine what an LD's experience of UTx is like. The reason for examining this now is twofold. First, many of the other ethical considerations regarding donors, such as motherhood status, relationship to recipient, and compensation, revolve around transplants using LDs; hence it is important at the start to understand what those donors are undergoing. Second, given that LDs are currently being used in UTx research, and

given that LDs are used in other organ transplants, it seems unlikely that LDs will be banned entirely. Therefore, it is important to have the full picture of the process, or what the process might be, in order to better understand and discuss the role and relevant ethical considerations surrounding donors.[5]

A donor's experience lies at the intersection of a hysterectomy and an organ procurement. It is easy to simplify the donor's experience by equating it to a hysterectomy; however, the procedure is much more extensive and risky than that. The complexity of the procedure stems from the extensive vascular dissection that necessarily accompanies the removal of a uterus that will be transplanted (Brännström et al. 608-609). The surgical risks of this type of uterine removal are as follows: hemorrhage (1%), transfusion (2% -12%), infection (fever of unknown origin [10% -20%], surgical site [6.6% -24.7%], wound site [4% -8%], pelvis [3.2% -10%], urinary tract [1.1% -5%]), pneumonia (0.4% -2.6%), bladder injury (1% -2%), intestinal injury (0.1% -1%), ureteral injury (0.1% -0.5%), and vesicovaginal fistula (0.1% -0.2%) (Kisu et al. 1408; Harris). In addition to these risks, a donor undergoes a long surgery, anywhere from 5-13 hours, to remove the uterus, which bears its own risks of general anesthesia and general surgery risks, and then has about a six-month recuperation period (Sifferlin, "4 Breakthrough Uterus Transplants"; Lavoué et al. 271).

In addition to these surgical risks, there are psychological risks or burdens associated with a uterine donation. Loss of gender identity and sexual dysfunction have been cited as consequences in both hysterectomies in general and uterine donations in particular (Williams 418-419). This sexual dysfunction often includes decreased libido, difficulty with lubrication, and denervation of the vagina, leading to reduced sexual

[5] For the sake of simplicity, in this section I use the term donor to refer to living donors exclusively

pleasure (Katz 65-66). Psychological risks associated with organ donations in general, which would possibly also be associated with uterine donation specifically, include depression, increased suicidality, and stress due to financial strain (Schover et al. 1598). We do not yet know the exact risk of each of these for uterine donors, a piece that will need further examination and research as this procedure moves forward, but it is safe to assume that the risks of these will parallel what has been observed in hysterectomies and other organ donations.

Two other pieces of the donor's experience that are important to note are the effect on child bearing and the onset of menopause. Neither of these can be classified as risks because they are the de facto outcomes of the procedure just as they are with a hysterectomy.[6] When a donor's uterus is removed, she will no longer be able to conceive, gestate, and bear a child. This fact may be obvious, but nevertheless is important to point out. This procedure is irreversible, and therefore the inability to bear a child is irreversible, unless the donor were to undergo a UTx as a recipient. The onset of menopause is a natural consequence of undergoing a hysterectomy. If ovaries are left, as would probably be the case for a UTx donor, this process may occur more slowly, but will still proceed ("Abdominal Hysterectomy"; Gallicchio et al. 1432). Menopause itself is often associated with chills, night sweats, hot flashes, slowed metabolism, mood changes, osteoporosis, etc. ("Menopause"). All of these outcomes occur naturally when a woman enters into menopause; they just may be triggered sooner than would occur if a woman reaches menopause naturally.

[6] Both of these outcomes are only applicable and relevant for women who are premenopausal, an element that will be examined in a subsequent section.

As is the case with any surgery, informed consent is of the utmost importance. In fact, the requirement of a donor's informed consent is the final point in the second section of the Montreal Criteria: that the donor must be "responsible enough to consent, informed enough to make a responsible decision, and not under coercion" (Lefkowitz et al., "An Update of the Montreal Criteria" 924). Williams states that much of the aversion to using LDs is due to the "possibility that living donors in UTx may be used in instances where – due to poor institutional procedures/safeguards, and/or despite appearances to contrary – their consent to donate is not fully informed and/or wholly voluntary" (Williams 422). While I do not believe that informed consent alone answers the question regarding the appropriateness of LDs, I believe it is a key piece of the discussion of whether or not LDs, or particular types of LDs (e.g. premenopausal women, relatives, etc.) can be considered as appropriate UTx donors.

It is important to note that in order to get informed consent according to clinical standards, the donor must be made aware of all the reasonable potential risks. This understanding is not limited to just the surgical risks; the education must also encompass the psychological risks and the full breadth of the outcomes of donation (Kisu et al. 1408). For example, it has been found that the risks of sexual dysfunction are unlikely to be discussed with hysterectomy patients, and for those patients who are counseled on these risks, most discussions only focus on immediate pre- and post-surgery effects, rather than on the long term effects (Katz 65). This indicates a lack of true informed consent in those hysterectomy patients due to an insufficient disclosure. Informed consent from UTx donors must ensure, to the best of a provider's abilities, that the donor is provided with all the information necessary to understand the surgical risks associated

with the procedure, the psychological risks of organ donation, the psychological and sexual risks of a hysterectomy, and the expected outcomes/effects of the procedure and what they mean for the donor.

This full picture of true informed consent is discussed throughout the next several sections. In order to begin discussing the ethics surrounding the motherhood status of the donor and the relational standing of the donor, we must first ensure that the donor is informed of what she may be undertaking. Furthermore, this understanding of informed consent is fundamental to the assessment of the appropriateness of the use of LDs on the whole and must be the starting point when answering the question whether or not the use of LDs is permissible.

ETHICAL CRITERIA TO EXAMINE

As in the previous chapter, the remainder of this chapter provides an ethical assessment of criteria for UTx donors, both those criteria that are already in place, as well as criteria that might be added. Any proposed additions to formal criteria will be assessed according to the ethical principles and concepts mentioned, and current criteria will be held to the same standards.

LIVING VS. DECEASED

The current criteria assume that it is permissible to use LDs. In fact, The Montreal Criteria makes no mention of the use of DDs. One major consideration to address when considering UTx donors, therefore, is whether it is permissible to use LDs at all and if so, whether it is morally preferable to use DDs. This seems to be one of the more divisive

questions in this field of research, yet it is absent from the criteria for selecting UTx donors. However, this is the defining difference between the two major trials in the United States. I examine three major pieces of these arguments: the medical factors, the risks to the donors, and the issue of supply and demand. After examining these three areas, I provide a recommendation regarding what research is still needed and for how to proceed when UTx moves into clinical use, both of which I expand upon in the final chapter.

Medical Factors

Many researchers cite various medical factors as reasons to allow, and even prefer, the use of LDs. While I cannot hope to delve into every medical factor involved in assessing living versus deceased uterine donors, I examine two of the main factors, the likelihood of success and the ability to perform adequate preoperative assessment. One underlying piece of the argument for those in favor of using LDs is that the majority of the animal studies on UTx used living animal donors (Williams 417). It is because of the animal studies performed, using animals ranging from rodents to primates, that the original Swedish trial used a LD when performing a UTx on a human (Brännström 69-70). That being said, this is not a compelling enough reason to push forward using LDs. If there are concerns about a lack of research with DDs, then this is an area that requires more research rather than a reason to use LDs.

The first medical factor that is often cited when arguing in favor of LDs is that it results in a higher likelihood of success. Part of this argument comes from a concern about blood supply to the organ prior to transplantation. Ischemic time is the time during

which an organ is without normal blood supply. Any transplant, even with a LD, will result in a certain degree of ischemic time; however, longer ischemic time carries risks of acute and chronic organ rejection (Kisu et al. 1407). As of now, the length of ischemic time that a uterus can withstand is unknown. This is an area that may require more research as this procedure moves forward. It is possible, however, that a uterus is likely to face longer ischemic time than other organs being harvested because of the nature of the procedure. Kisu et al. points out that because UTx is a quality of life transplant rather than a life-saving transplant, the uterus would be one of the last to be harvested from a DD, which would therefore result in longer ischemic time and therefore carry a higher risk of rejection (Kisu et al. 1407). Kisu et al. also points out that in other transplants using DDs, research has showed that death results in systematic inflammation, which may also contribute to risk of graft failure (Kisu et al. 1407). Neither of these arguments, however, actually stem from research in UTx. While some of these findings are likely to hold true for this procedure, they do not give the full picture to make a compelling argument.

One of the major complications leading to failure of this procedure is necrosis of the uterus. Necrosis is when an organ, in this case the uterus, does not receive adequate blood supply, ultimately leading to its removal. This was the reason that the very first UTx, performed in Saudi Arabia in 2000, failed. That recipient had complications with thrombosis 99 days following the procedure, which ultimately resulted in a necrotic uterus that required removal (Fageeh et al.; Brännström et al. 607). Studies following this failure in Saudi Arabia cited that using longer lengths of veins would help prevent thrombosis and necrosis, which would lead to a greater likelihood of success

(Johannesson and Enskog 1203-1204). While a longer length of uterine vessel is preferable for success of the graft, it is harder to obtain from a LD due to longer length of surgery and associated risks. Other studies found that just as longer lengths of uterine vessels helped increase the success of the surgery, using ovarian vessels instead of uterine vessels might also lead to greater success (Johannesson et al. 1224). The ovarian veins are wider in diameter and longer than the uterine veins, and thus can reduce the risk of thrombosis and necrosis (Kisu et al. 1408; Lavoué et al. 269). Using ovarian veins requires the removal of the ovaries, in addition to the uterus, which results in ovarian dysfunction and hormone imbalances if the donor is premenopausal. Using a DD, therefore, not only results in removing these particular risks to the donor, but also may enable greater success of the graft for the recipient by allowing the surgeons better access to remove longer lengths of vasculature.

Research in kidney transplants show that the use of LDs results in better long-term graft survival, which makes many conclude that the use of LDs in UTx would do the same and therefore be preferable (Davis and Delmonico 2098). That may be true; however, long-term graft survival might not actually be necessary. As discussed, UTx is unique in that it is an ephemeral procedure, with the graft being removed after one or two births. When the Turkish research team examined HLA matching, they found that without an HLA match there was no difference in 1-year and 5-year survival rates of the graft. Therefore, they concluded that even if there might be greater long-term differences in graft survival, this did not affect their research because they had no need to look beyond the 5-year survival of the graft (Ozkan et al. 474). A similar conclusion can be made here: even if a LD may increase long-term graft survival, researchers need not

worry about the survival differences past several years out, because the graft will have already been removed.

The second set of medical factors to be considered when assessing the use of living versus deceased donors is the degree of preoperative investigation that can be performed. The degree of assessment that is possible with DDs is very limited (Lavoué et al. 270). For a DD, most of the evaluation is performed via ultrasound, which cannot show all relevant potential abnormalities to the medical team. With LDs, on the other hand, an extensive preoperative workup can be performed. Because organ procurement from a LD is not limited by time, the examination can include both ultrasound and pelvic magnetic resonance imaging to ensure that the donated uterus is acceptable. Doctors can also assess whether cervical dysplasia and/or human papillomavirus are present in the uterus before the transplant occurs (Lavoué et al. 270-271). This extensive assessment may help ensure better graft survival and also may help guard against any factors that may inhibit fertility potential following a successful transplant (Williams 417). Finally, although there is less possibility for thorough assessment of the organ, using DDs may provide a greater range of donors. For example, it may permit the use of younger donors who would otherwise have not concluded their parity. The benefit of younger donors is that certain risks, such as preeclampsia, are alleviated (Lavoué et al. 270).

These medical factors are of the utmost importance when assessing the permissibility of living versus deceased donors. If one looks at success of the graft alone, it may seem simple to conclude that the use of LDs is preferable. Using LDs enables better assessment of the organ and better long-term graft survival. The latter, although not necessary, certainly is not a bad thing. However, success alone is not enough on which to

base a moral decision. These medical factors and their contribution to success must be viewed alongside other factors, such as the risks to the donor, in order to conclusively prefer living or deceased donors.

Risks to Donors

The risk to the donor is perhaps the most cited argument in favor of preferring DDs. The risks involved in being a uterine donor include both the physical risks during surgery as well as the potential for psychological harms following surgery. No surgery is without risk; however, as discussed in the first chapter, the difference with a transplant surgery is that the risks are not accompanied by potential benefits for the donor (except for potential psychological benefits of helping a loved one or stranger). Researchers, medical teams, and ethicists participating in and examining organ procurement in LDs must closely examine the principles of nonmaleficence and beneficence. Because of the potential benefit garnered by the recipient, physicians have a duty to minimize the harm inflicted on donors.

The physical risks of donation have already been discussed earlier in this chapter. These risks are relatively easy to determine and assess. The psychological risks, however, are harder to assess currently, as UTx is still in the research phase, and has been little psychological follow-up with the LDs. However, examining the potential psychological harms following hysterectomies and other organ donations forms a picture of what will probably be the case following a uterine donation. Because of the nature of the organ, hysterectomies carry risks of changes in body image, including loss of gender identity, and changes in a woman's sexual relationships (Peterson 514). The potential for and

extent of these effects largely depend on the reason for the hysterectomy in the first place; therefore, some may not apply to a UTx donor (Peterson et al. 520). If LDs were to be continued being used, the subsequent psychological effects would need to be studied in order to help mitigate them.

All organ donations are associated with various psychological risks. These can include some risk of depression and/or suicidality. Following kidney donation, 7% of LDs experienced depression and 4% were disappointed with the overall experience (Schover et al. 1598). Furthermore, if the graft failed for the recipient, 43% felt that their role made the experience more devastating, and 11% experience suicidal ideation (Schover et al. 1598). With regard to UTx, this experience probably would apply not only if the graft failed, but also if the recipient were unable to conceive or bear a child. It seems a probable potential risk to be weighed when considering LDUTx and should be studied as a part of LD follow up.

Given all of these risks and the "lack of safety data", the International Federation of Gynecology and Obstetrics (FIGO) has stated that it is not only morally permissible to use DDs, but also that it is ethically inappropriate to use LDs in general ("Uterine Transplantation", 270). Their statement, however, does not address why retrieval of a uterus from a LD is significantly different from retrieval of a kidney from a LD, which leaves their argument incomplete. In response, Del Priore and Gudipudi appeal to the non-essential nature of the uterus transplant as compared to a kidney transplant, stating that "the transplant community would never consider a LD for anything less essential than a kidney or part of a liver" (Del Priore and Gudipudi 22). This argument concedes that certain risks are acceptable when the potential benefit for the recipient warrants it,

and then concludes that the benefit for the recipient of a UTx is not enough to justify the risks imposed on the donor.

As mentioned, any medical procedure has associated risks, and the presence of risks does not mean that an individual cannot undergo any procedure, when the benefit is primarily or exclusively for others. In health care, we allow people to undertake risks according to two concepts: risk-benefit ratio and respect for autonomy. Risks can be undertaken when the potential benefits of the procedure outweigh the risks. With UTx, we must examine the aggregate risk-benefit ratio to assess if the potential benefits for the recipient outweigh the risks for the donor. The aggregation of the risks and benefits is more closely examined in the conclusion of this section. Although there are many risks to the donor, there are also great potential benefits for the recipient of UTx, which may permit the use of LDs. However, there is an alternative to using LDs in UTx, and at this point, there is no greater potential benefit achieved from LDUTx than from DDUTx. This alternative, with equal potential benefits, changes the aggregate risk-benefit ratio, and may allow for the prohibition of living uterus donors because of the risks for the donor. Furthermore, as Del Priore and Gudipudi point out above, although there is considerable benefit for the recipient, this benefit is considered less significant than the benefit granted by a kidney or liver lobe transplant.

The second concept that allows an individual to take on the risks of a procedure is respect for autonomy. As mentioned in both the introduction and the discussion of the motherhood status of the donor, respect for autonomy on its own allows a woman to make an informed decision to take on all of the aforementioned risks and undergo the surgery to donate her uterus. Although it is true that respect for autonomy, achieved

through informed consent, could render the risks acceptable, this principle does not stand alone. Given the principles of nonmaleficence and beneficence, and the concept of the risk-benefit ratio, even when a woman gives her informed consent to serve as a LD, it still may not be ethically appropriate for the medical team to perform the LDUTx.

Supply & Demand

Despite the risks that are imposed on a living UTx donor, many argue in favor of using LDs out of a fear that the demand by potential UTx recipients will greatly outweigh the number of uteri that DDs can provide, which therefore means that LDs should be used to close the gap. Two questions come to mind upon hearing this argument: 1) How do we know that the demand will outpace the supply of uteri donated by DDs? 2) Can a lack of supply justify the use of LDs?

Researchers have begun to try to assess what the demand for UTx will be and how that compares to a potential supply by DDs. In a systematic review of uterus availability, researchers found that the availability of viable deceased uterine donors may vary depending on geography and selection criteria. Two studies, one in New York and one in France, had diverging accounts. In New York, researchers found that using very general selection criteria (16-45 years old, specific consent for uterus retrieval, healthy uterus, etc.), there may be "many potential donors;" however, they note that with these criteria there is greater risk of vascular disease, which may impede graft success. If they were to limit their selection criteria, however, to select for younger donors to limit that risk, the donor pool is significantly reduced and may not meet the demand (Lavoué et al. 271). In the study in France, on the other hand, the French Biomedicine Agency stated

that the availability of young DDs was adequate to meet the demand of UTX (Lavoué et al. 271). As Lavoué et al. note, however, there are very few data on what exactly the demand for UTx will be; therefore, regardless of the assessment of the potential supply of uteri, it is hard to say definitively that supply will meet the demand. I think that further research needs to be conducted as UTx moves forward to determine more precisely what supply and demand for this procedure is. With the current data, it is misleading to state that there certainly is not a large enough supply of uteri from DDs; therefore, citing a lack of supply of DDs right now is not sufficient to move toward the use of LDs.

Putting aside the current supply and demand for this procedure for a moment, we must also determine if a lack of supply, if found to be true, would be enough to justify the use of LDs. In other words, if we did in fact currently have adequate data that showed that the demand for UTx greatly outpaced the supply provided by DDs, would it be ethical to begin using LDs? I think that an issue of supply and demand on its own is not morally compelling enough to justify moving towards the use of LDs. Rather than looking to supply and demand as an argument regarding whether or not it is permissible to use LDs, we must address the question of permissibility based on the principles at play: nonmaleficence, beneficence, autonomy, justice, and risk-benefit ratio. Once a decision is made, if there is a discrepancy in supply and demand, we can then address that issue separately based on those same principles. Based on what has been seen in other organ transplants, it is likely that the demand for UTx will outpace the supply of uteri, *even if* LDs are used. The question of how this discrepancy should be handled will be addressed in Chapter 4 as an issue that merits further discussion as UTx progresses.

Given all of these elements: medical factors, risks to the donor, and potential problems of supply, I believe that it is morally preferable to use DDs. Furthermore, I believe it is ethically *impermissible* to use LDs *unless* research with LDs shows significantly greater success, with success defined *not* by graft survival, but by pregnancy and live birth rates. Williams argues against FIGO's statement by appealing to the fact that we use healthy volunteers, who are exposed to risks and for whom there is no individual benefit, in clinical trials and we use LDs in kidney transplants. Therefore, Williams claims that at this stage of research, as long as there is informed consent and a favorable aggregate risk-benefit ratio, it is acceptable to use LDs (Williams 419-420, 424). Although it is true that we use healthy volunteers in research and LDs in kidney transplants, there are enough ways in which UTx differs from each of those, in ways that makes the aggregate risk-benefit ratio unfavorable, to be able to logically say that, at this time, it is impermissible to use LDs.

UTx in clinical practice differs greatly from clinical trials in the overall benefit achieved. The goal of clinical trials is to gain generalizable knowledge, whether about a disease state, a medicine, or other factors, to help *many* future individuals. In research, therefore, the risk-benefit ratio of using healthy volunteers is acceptable because of the scale of the benefit garnered by the research, whereas, with UTx being used as a treatment, the risks taken on by a LD only grant benefit to one individual, the recipient of the uterus; therefore, the risk-benefit ratio is drastically different.

UTx differs from kidney transplants in the nature of the procedure and the definition of a successful procedure. As discussed, unlike a kidney transplant, UTx does

not require long-term graft survival, nor is long-term graft survival an acceptable definition of a successful procedure in this case. Because of the ephemeral nature of the procedure and the different definition of success, when examining the aggregate risk-benefit ratio, the risks being relatively equal between a living kidney donor and a living uterus donor, the benefit of using a living uterus donor is not as great as the benefit of using a living kidney donor. Furthermore, unlike the kidney, the uterus is tied to a donor's identity and therefore carries additional potential psychological harms (Lefkowitz et al., "The Montreal Criteria" 443). This too changes the aggregate risk-benefit ratio of a living uterus donor as compared to a living kidney donor. These differences in the aggregate risk-benefit ratio are enough to call into question the comparison between living kidney and uterine donors. Therefore it is in fact acceptable and logical to allow the use of LDs in kidney transplants and disallow the use of living donors in UTx. If future research, discussed in the final chapter, were to show that using living uterus donors increases the possibility of success, as defined by pregnancy and live birth rates, however, the aggregate risk-benefit ratio would shift and may allow for the use of LDs.

Lastly, as mentioned in the previous section, I do not believe that potential lack of supply is a compelling reason to use LDs. I realize that by disallowing the use of LDs, the supply of donated uteri is significantly limited. That being said, the pragmatism of meeting demand cannot trump ethics in making this decision. In the next chapter I discuss how to ethically address issues of inadequate supply, but that discussion lies outside the moral permissibility of using LDs.

Although I believe that using LDs is impermissible in clinical practice, current criteria allow it. Therefore, it is still important to assess the current criteria involving LDs to ensure that if LDs continue to be used, LDUTx will be done in the most ethical manner possible. The following sections, discussing age and motherhood status, relationship to the recipient, and compensation refer to the clinical use of LDs, therefore when "donor" is used, it is referring to LDs specifically, unless otherwise indicated.

AGE & MOTHERHOOD STATUS

Age and motherhood status were considerations examined with regard to UTx recipients. With recipients, these each served as distinct considerations; however, with donors, these two criteria are all but inextricably tied together. As such, I discuss age and motherhood status simultaneously.

In Chapter 2, I discussed whether women who are already mothers or who are beyond the "normal" childbearing age are appropriate UTx recipients. In this chapter, however, the question is almost flipped: Are nulliparous women (women who have never given birth) or women of childbearing years (either with or without children) appropriate UTx donors? The Montreal Criteria addresses this somewhat it points 2a and 2b1, stating that the woman must of reproductive age with no medical contraindications to donation and must have repeatedly attested to her conclusion of parity (Lefkowitz et al., "An Update of the Montreal Criteria" 924). Similarly in their guidelines, FIGO's Committee for the Ethical Aspects of Human Reproduction and Women's Health stated that: "it is unethical to remove a uterus for transplantation from a young woman who did not complete having the desired number of children" ("Uterine Transplantation", 270).

At face value, each of these recommendations seems easy to agree with. It would be unethical for a provider to remove a uterus from a woman who still wants to use it to have children, and if a woman has repeatedly made it known that she does not want to have any more children, you can conclude that she no longer has a need for her uterus ("Uterine Transplantation", 270; Lefkowitz et al., "An Update of the Montreal Criteria" 924). Each of these statements, however, oversimplifies all of the ethical questions at hand. One question at the heart of examining this topic is: how can one be sure that a woman does not wish to have any or more children? As important as this question is, however, it is also a question to be cautious about, because clinicians may act paternalistically by refusing to believe that a woman has actually concluded having children or has chosen not to have children.

One major reason that providers and surgical teams shy away from accepting UTx donations from women without children or with just one or two children is fear of regret on the donors' part.[7] The writers of the Montreal Criteria cite the fact that many men who have gotten a vasectomy are grateful for and take advantage of the fact that it can sometimes be reversed (Lefkowitz et al., "The Montreal Criteria" 443). Even the mention of this in that discussion illustrates the deep fear associated with the irreversibility of a UTx donation. This fear seems to stem from a desire to act nonmaleficently. The fear is of harming the donor in the future by denying her the experience of pregnancy and ability to have a child.

Nonmaleficence, however, is not an absolute, but a *prima facie* principle and it therefore must be balanced against other ethical principles. In this case, respect for autonomy needs to be closely inspected and weighed against this concept of

[7] Another reason for using a donor who has had children is that the uterus has proved itself capable of gestation.

nonmaleficence (Lefkowitz et al., "An Update of the Montreal Criteria" 925). Respect for autonomy dictates that individuals have a right to make decisions for themselves, and doctors have an obligation, although not absolute, to honor these decisions (Beauchamp and Childress 99-102). This principle means that nulliparous women or women with few children, have the ability to make an informed decision that a doctor has a duty to respect and uphold.

The fear of failing to act according to nonmaleficence may come from deeply embedded pronatalism in society. The average number of children in a family, according to the United States Census Bureau, is 2.54 (as of 2017). As the average, this easily becomes viewed as "normal." It is not improbable to think that when providers consider women who fall below this average, they feel that they would be depriving them of a normal life by honoring their decision. This, however, imposes a very particular definition of family on these women, one that they may not actually desire.

That being said, the fear of regret and irreversibility is not entirely dishonorable. Part of respect for autonomy is ensuring that decisions are adequately informed and are free from coercion and undue influence. When examined under the concept of the risk-benefit ratio, the irreversibility and the riskiness of this procedure mean that the obligation to ensure both of these aspects of autonomous decision making is great, and therefore may call for a high burden of proof. As discussed, to ensure that a decision is fully informed, the medical team needs to ensure that all of the aforementioned topics (surgical risks, psychological risks, future inability to have children, etc.) are fully disclosed and understood. Lefkowitz et al. suggest ensuring that all information regarding donation is divulged and that the potential donor is given time to assess this information

(Lefkowitz et al. 443). If a donor demonstrates understanding to the medical team after time of assessment, the decision can be deemed adequately informed. To ensure that the decision is not coerced, the woman must demonstrate that her lack of desire for [more] children is her own and is free from coercion.

The exact way in which a woman can demonstrate that this desire is her own is a topic that must be continually examined as UTx moves forward. The Montreal Criteria make mention that an LD must repeatedly attest to this fact, but what exactly does that mean? Does she need to have made more than one mention of it to friends? Does she need to have already explored options of concluding parity previously? Perhaps she must put her desire in writing and if in a year her decision remains, then she can serve as a donor. I worry about putting the burden of assessment solely on the medical team, leaving them to decide on a case-by-case basis. I believe that this would probably lead to women's decisions not being upheld due to the deeply embedded pronatalism of society.

One way in which the question of a LD's desire for children is avoided is if the woman is post-menopausal. In these cases, regardless of a woman's motherhood status, her body naturally no longer has the ability to conceive and bear a child, essentially making the decision for her and for the doctors. If a postmenopausal uterus can be used, no one is taking away a woman's chance to have a child naturally. In order to examine this potential situation, I first examine the medical implications of using a postmenopausal uterus, and then I examine whether or not this is a preferable type of donation.

Perhaps the most important fact about older uteri to mention at the outset is that even though postmenopausal women cannot become pregnant naturally, a

postmenopausal uterus itself is still able to achieve pregnancy. As older IVF mothers and older surrogates have demonstrated, older uteri have the endometrial receptivity needed to allow conception and gestation (Johannesson and Enskog 1204). Furthermore, the potential for use of postmenopausal donors was demonstrated in Brännström's trial, where several of the LDs were postmenopausal and the mean age was 53 years old (Lavoué et al. 270). In Brännström's trial, the functionality of the uteri, whether pre- or post- menopausal, was assessed by prescribing an oral contraceptive pill and determining that menstrual activity occurred normally (Brännström et al. 608). This test for functionality found that under an appropriate hormone regimen, a postmenopausal uterus had the same ability to gestate a child as a pre-menopausal uterus. Furthermore, unlike the uterus of a nulliparous woman, the uterus of a postmenopausal woman who has had children has demonstrated that it is able to carry a pregnancy (Brännström 70). Of course this is also true for the uterus of a woman who has had children already but has chosen to conclude her parity.

Another benefit of using a postmenopausal donor is that the ovarian veins can be removed and used for a more effective transplant (Kisu et al. 1408). These veins are longer and wider than uterine veins, which is preferable for anastomosis. In order to remove the ovarian vein, however, the ovaries have to also be removed, which would lead to greater hormone dysfunction in both premenopausal and postmenopausal women (Kisu et al. 1408; Lavoué et al. 269).

Despite these potential benefits of using a postmenopausal uterus, there are also risks. Despite having used older uteri in his study, even Brännström notes that older uteri may be associated with certain risks. He notes that using older organs may be associated

with increased risk of preeclampsia in pregnancy (Brännström et al. 615). He also states, however, that the exact reason for and degree of this are unknown; hence it is hard to assess exactly what the risk is of using older uteri. However, even though the exact risks are unknown, the risks contribute to the overall risk-benefit ratio, and therefore there is a general preference for using younger organs (Brännström et al. 615). This is another aspect of UTx that must continue to be researched in order to further assess whether there should be a preference for postmenopausal donations.

Aside from a possibly increased risk of preeclampsia, there do not seem to be any additional risks when using a postmenopausal uterus versus a premenopausal uterus. Due to the risk of regret and the duty of nonmaleficence discussed previously, and due to the lack of additional risks and even potential benefits of a postmenopausal uterus, the use of postmenopausal donors should be preferred to the use of premenopausal donors (when examining LDs).

One question that this raises, which we discussed when examining LDUTx versus DDUTx, is what if we do not have a great enough supply of a certain type of organs to meet the demand (i.e. what if we do not have enough postmenopausal donors, is it then permissible to use premenopausal donors?). As discussed, a lack of supply is not weighty enough to dictate the moral discussion. The general conclusions here are as follows: Medical teams need to respect women's autonomous decisions to donate their uteri, even if they have no or few children. However, there needs to be a high burden of proof that a woman has in fact concluded having children in order to ensure that the decision is fully

informed and autonomous and that the doctors are acting with nonmaleficence. Additionally, if and when LDs are used, there should be a preference for using postmenopausal donors.

RELATIONSHIP TO PATIENT

In addition to motherhood status and age, the donor's relationship to the patient is an important ethical consideration with regard to LDs. As in the previous section, when "donor" is used, it will refer specifically to LDs. As mentioned in the first chapter, there are several types of donations when considering the relationship between donor and recipient. One main category is whether or not the donor is related to the recipient. Similar considerations can be applied to donors who are close friends of the recipient, even if they are not related. Another category of donation is whether the donor is identified or unidentified, in other words, does the recipient know who the donor is (regardless of whether they are related or known personally to the recipient)? Donations can also be either directed or non-directed, meaning the organ is either intended to be donated to a specific individual or it is donated to anyone in need (Truog 444).

Within these categorizations, I focus on the considerations that apply to related donors, those that apply to unrelated/altruistic donors, and those at play with regard to whether or not the donor is identified. Although these categories are not specifically mentioned in current UTx criteria, they are relevant for two important reasons. The first is that the relationship to the patient is pertinent to point 2d of The Montreal Criteria which requires that the donor "is responsible enough to consent, informed enough to make a responsible decision, and not under coercion" (Lefkowitz et al., "An Update of

the Montreal Criteria" 924). The second reason it is important to assess the relationship of the donor to the recipient as a potential criterion is to see the potential effects the relationship has on the experience of both the UTx recipient and the future child.

Related Donors

The first question is whether a genetic relationship between donor and recipient leads to a greater chance of success. In Brännström's trial, there was a preference for the donor to be genetically related to the recipient, because there can be a closer match between the human leukocyte antigen (HLA) markers of an organ donor and recipient if they are biologically related (Brännström et al. 614). With traditional organ transplants, the HLA matching is important to achieve better long-term graft survival and function. If HLA markers are more similar, the body is less likely to recognize the organ as foreign and therefore is less likely to reject the graft. That being said, UTx does not need long-term graft survival because it is an ephemeral procedure. In a study of liver transplants, researchers found that HLA mismatching had very minimal effects on five-year graft survival rates (Ozan et al. 474). Assuming that HLA mismatching would affect UTx the same way it was shown to affect liver transplants, the mismatching would not have a large effect on the survival of the graft before it was removed. This does of course assume that the 1-2 pregnancies are achieved quickly, but having the transplant for five years does fall in line with the overall intention for the procedure. If then, there is no great benefit garnered from the donor's genetic relationship, what other considerations are relevant in assessing this relationship?

As mentioned in the previous section, informed consent free from coercion is of the utmost importance in UTx and a piece of part 2d of The Montreal Criteria. Generally consent is not just classified as either coerced or not; the analysis is much more nuanced. In a study of informed consent of living related liver lobe donors, there were three major patterns of consent found: unconditional, pressured, and with ulterior motives. Unconditional consent is associated with an overzealous agreement where the information is hardly listened to because the decision to help a family member has already been made, regardless of the risks. Pressured consent is when donors feel they have obligations toward their family member, which overrides the fear they have regarding the information given. Ulterior-motivated consent is when consent is given not out of love but out of a desire for a particular set of repercussions, perhaps to have the recipient indebted to the donor (Fujita et al. 1426). In looking at each of these categories of consent, it is hard to know which, if any, are appropriate and true iterations of informed consent and voluntariness (Biller-Andorno 618).

Of the categories of consent, the unconditional consent seems to be the closest to a decision made free from outside forces, but is it actually? In a study of parental liver lobe donors, the medical team found that "it [was] impossible for parents to give truly informed and free consent" (Nilsson 373). Although these parents may not feel overt pressure, nor would they themselves state that they were feeling pressure, nonetheless, their close relationships apply pressure to donate. Dickens asserts that this implied pressure probably extends beyond life-saving procedures, even to a quality of life procedure like UTx. Statements from mothers like "there is nothing they would not do" to help their daughter conceive indicate that their consent is not entirely free from

pressure (Dickens 126). Knibbe et al. argue that this feeling of a lack of choice on the part of family members may not indicate coercion, but may just be indicative that their relationship is a strong motivating factor (Knibbe et al. 435). The fact that pressure exists does not mean that donations from relatives should be prohibited due to a lack of voluntariness, it merely means the medical team needs to exercise caution during the consent process to ensure that the donor is has been given all relevant information to understand of all of the risks and the implications of these risks. Biller-Andorno suggests several ways to ensure voluntariness during the informed consent process, which she calls "procedural safeguards". These include making sure the potential donor has opportunities to say no while assuring the donor of confidentiality if he or she chooses to withdraw. She also suggests including an independent donor advocate in the decision making process (Biller-Adorno 618). Although voluntariness hinges on the individual donor's being self-interested, an individual's interests are inextricably tied to the interests of her family (Knibbe et al. 435). In the case of UTx, the medical team must make sure the donor is able to give informed consent and that her decision is voluntary; however, the team must also understand that the emotions involved and the process of consent when donating to a family member may look different from donating to an unrelated recipient.

In addition to the pressures that a related donor might feel to donate, there are pressures that the recipients may feel if they have received a uterus from a family member. Financial compensation, a topic that is discussed later, is not the only type of reciprocity that can stem from a gift as monumental as an organ. While compensation is relatively easy to monitor between strangers, it is very difficult to assess between family

members (Dickens 126). If a family member, whether mother, aunt, sister, etc., donates her uterus, there may be an expectation that something will be given in return. This may be a physical or financial gift, a grandchild, or a certain type of relationship with either the recipient or the future child. While this type of gift expectation is not necessarily wrong, these reciprocal gifts are hard to monitor between family members, and the familial relationship makes it difficult to predict the psychological effects of these expectations (Lavoué et al. 270).

Altruistic/Unrelated Donor

UTx donations from unrelated (altruistic) donors, whether directed, non-directed, identified or unidentified, carry their own sets of cautions and ethical considerations. With life-saving organ donations, the donor is assuming the known risks in order to try to save a life, even a life of an unknown individual. UTx, on the other hand, is not a life-saving procedure; therefore the motives of an altruistic donor are somewhat different (Dickens 126). This does not suppose that there is no good or ethical reason for an altruistic uterine donor. Perhaps the woman had a family member suffer from a similar condition or just feels drawn by the stories of other women and is herself done having children; both are potentially good and valid reasons to donate. However, because the potential motive is less clear, the medical team needs to ascertain that the donor is able and informed enough to consent and is not being coerced (Lefkowitz et al., "An Update of the Montreal Criteria" 924).

One motivation that often causes concern, and which has led to heated debates, is that of compensation. I address this topic in the next section of this chapter and therefore

will not discuss it in full here. Compensation can mean many different things, and applies differently to related and unrelated donors. It is widely, although not universally, held that altruism should be the driving motivation for organ donation. In a study examining the motivations of individuals willing to be organ donors, all of the participants cited altruism, whether to save lives or to contribute to medical knowledge, as their chief motive (Sanner 1149). Because of the emphasis on altruism, compensation as a donor's driving motivation is often called into question and viewed as inappropriate. Additionally, those concerned about compensation as a driving motivation bring up the fact that this might indicate that a vulnerable individual or population is not able to make an adequately voluntary decision and may be subject to exploitation for their organs (Friedman 747).

One precaution that may be used when assessing motives is to subject the potential donor to a psychological assessment. This assessment is intended to make sure that the potential donor is not just medically able to donate, but is also responsible and informed enough to make the decision. No psychological assessment is perfect, but assessment can help the medical team determine whether the potential donor is of sound mind and able to consent according to The Montreal Criteria.

Identified vs. Unidentified

The final consideration regarding altruistic donors is whether they can or should be anonymous. Although this is not addressed in the current criteria, it is worth considering whether it should. One benefit of anonymity is that it potentially avoids certain psychological effects on the recipient (Lavoué et al. 272). Many organ recipients

cite the guilt that they feel for subjecting another individual, especially one unrelated to them, to such great risks and burdens, and view the donation as an "unpayable debt." Lavoué et al. examine whether this feeling of guilt and debt would be lessened or deepened with UTx. They speculate that on the one hand, the organ is not a vital organ, therefore the risk is more difficult to justify, which may lead to a deeper sense of guilt. On the other hand, assuming the donor has concluded parity, she is no longer in need of their uterus, which may lessen the sense of guilt (Lavoué et al. 272). The effects of anonymity, or lack thereof, is a topic that should be further researched and discussed as UTx moves forward, but for now, in my view, both identified and unidentified donations are permissible.

Because UTx is not simply an organ donation, but it also serves as an ART, there is another question to address when examining the appropriateness of anonymous donors. In her paper, "Gametes or organs? How should we legally classify ovaries used for transplantation in the USA?", Lisa Campo-Engelstein addresses ovarian tissue transplants (OTT), and whether we should treat them like organ transplants or like gamete donations. For several reasons, she makes the recommendation that they be classified as gamete donations. The largest reason she cites is that the intended result of OTT is pregnancy and a child, as is the case with UTx. Part of this recommendation is then that there is certain information that the ovarian tissue donor must disclose, therefore not remaining *fully* anonymous (Campo-Engelstein 168-169). The question is then, if it is impermissible for an OTT donor to remain fully anonymous because of the goal of the procedure, should a UTx donor disclose her identity? I do not believe that this needs to be a criterion when assessing UTx donors. There are two ways in which UTx differs from OTT, which in

turn make anonymity of donation permissible. The first reason is that UTx treats only one condition. OTT can treat both infertility and early onset menopause (Campo-Engelstein 166). This is important because the donation may not have been intended to provide the recipient with a child. In such cases, if a pregnancy is achieved due to OTT, this would violate the donor's right *not* to reproduce (Campo-Engelstein 169). UTx, on the other hand, is used to treat only UFI, which means that the donor's intention by definition allows the transplant to be used as a fertility treatment. Another reason that Lisa Campo-Engelstein classifies OTT as a gamete donation is the genetic relationship between OTT donor and future child of the recipient (Campo-Engelstein 168-169). While the ultimate goal of both OTT and UTx may overlap, to achieve pregnancy and have a child, the role the procedures and the tissues/organs play in achieving this goal is vastly different. Unlike OTT, UTx will not result in a genetic relationship between donor and future child, because the uterus simply serves as a vessel for the pregnancy. Because there is no potential for genetic relationship between donor and future child, there is no basis to prohibit complete anonymity.

Of all of the categories of relationship between donor and recipient, directed donation to a loved one or friend, non-directed donation, to a recipient who may be either identified or unidentified, and directed donation to a stranger, none are categorically inappropriate; therefore, the criteria for selecting donors does not need to include any directives regarding a donor's relationship to the recipient. However, each type of relationship between donor and recipient carries its own set of considerations, from

giving a family member all the information to understand all of the risks to assessing the motives of an altruistic donor. The medical team must be aware of the relevant considerations of each type of relationship to handle the donation in an ethical manner.

COMPENSATION

Compensation is a widely debated topic in both the organ transplant and ART communities. Discussion of compensation is inextricably linked to the ethical selection of UTx donors. There are three important things I consider in this section. First, this section is focused on compensation for living donors. I touch briefly on whether compensating the living relatives of deceased donors, is permissible, but my primary focus is on compensation for living donors. The word "donor" in this section refers to living donors unless otherwise specified. Second, laws and regulations on compensation vary from country to country. I discuss only the current state of laws and related recommendations for the United States. Third, the goal of this section is not to argue for or against any of the current laws or regulations on compensation for organ donations or ARTs. I review the current regulations for compensation for organ donation and ARTs and then give my recommendation for where UTx fits in. As we have discussed, UTx is an organ donation being used as an ART; however, because regulations on compensation differ greatly between organ donations and ARTs, UTx must be classified as either one or the other in this area or it must be determined to be different enough from both to have a unique set of regulations.

Current Laws

As discussed in Chapter 1, according to the National Organ Transplantation Act, donors are prohibited from receiving "valuable consideration" for the organ (National Organ Transplantation Act). In essence, this means that payment for organ donation is illegal, but coverage of certain expenses may be permissible. Generally the recipient's health insurance will pay for a living donor's immediate medical expenses, but the donor cannot be paid for either the organ or the donation itself. As mentioned, donors are often responsible for paying for their travel to and from the various medial appointments and procedures, and are not compensated for lost wages due to the surgery and subsequent recovery (Friedman 746).

Compensation for ARTs differs according to the type of ART. Payments for gametes (sperm and eggs) are routine and generally acceptable (Almeling 37). As mentioned in the first chapter, however, what is an appropriate payment for gametes is debated, especially when it comes to egg donation. ASRM recommends that payments above $5,000 require justification and any payments above $10,000 "go beyond what is appropriate" ("Financial Incentives in Recruitment of Oocyte Donors", S243). Payments above this upper limit may be classified as undue inducement, which is prohibited in order to help prevent exploitation of vulnerable populations. Part of the ASRM recommendation, however, is that allowing for some payment beyond compensation for medical expenses is beneficial because it helps donors, especially egg donors, understand the real physical risks and emotional burdens of the donation ("Financial Incentives in Recruitment of Oocyte Donors", S241).

Compensation for surrogacy varies greatly from state to state. There are no federal laws pertaining to the enforceability of surrogacy contracts nor are there laws forbidding compensation of surrogates (Watson 532). Some states expressly forbid any type of compensation to surrogates. In other states, however, while compensation is not specifically prohibited, any type of compensation would render a surrogacy contract unenforceable if there was a disagreement between the surrogate and the intended parents (Watson 533-534).

Recommendation

In terms of compensation in clinical use, UTx should be classified as an organ donation and subject to the same laws as any other organ transplant. This is my recommendation for three reasons, discussed below: 1) the ties of the donor to the future child 2) the immediate goal of the donation and 3) the risks to the donor. Although I have described UTx as an organ donation being used as an ART, I believe that the three reasons listed above make it more similar to an organ donation with regard to compensation. Furthermore I do not think that the differences between any other organ donation and UTx render UTx as deserving of an entirely separate set of regulations and governance.

Donor's Ties to Future Child

The first reason that UTx should be treated according to organ donation regulations is that the donor's ties to the future child are different from the ties of either a gamete donor or a surrogate. Although there is anecdotal evidence that organ donors and their families

feel tied to the recipients, this tie is an emotional one rather than a genetic or gestational relationship (Earl; Flam). Any genetic ties between donor and future child only exist if they pre-date the donation. For example, if a mother donates her uterus to her daughter, the future child will be the donor's grandchild. In this case, however, if the donor were not used, either because the daughter conceived naturally or because a different donor was used, the genetic tie would still remain between mother and future child as grandmother and grandchild. With a gamete donor, on the other hand, the donation itself creates a genetic tie. For example, if a Woman A donates her eggs to Woman B, the future child of Woman B will be genetically related to Woman A, but if Woman A was not the egg donor, either because Woman B conceived naturally or because a different egg donor was used, Woman A would not be related to Woman B's child. If an unrelated uterine donor is used, however, the donor will have no genetic relationship to the future child. For example, if Woman A donates her uterus to Woman B, the future child is not related to Woman A. Uterine donation also does not imply a gestational relationship between uterine donor and future child. Although the gestational organ is used, the donor is not the one gestating the future child, as would be the case with surrogacy.

Therefore, although there still may be a tie, or even a relationship, between the donor and the future child, it is weaker than that of a surrogate or gamete donor. Because of the type of tie that exists between uterine donor and future child, the psychological effects of undergoing the procedure are different. This does not mean that the psychological effects are minimal. On the contrary, there are serious potential psychological effects. These effects, however, are more like the potential psychological effects of acting as an organ donor, than they are like the effects of acting as a gamete donor or surrogate. Therefore,

part of the reason compensation for donating a uterus should be considered the same way it would for any other organ donation is because of the weakness of the tie between donor and future child and the corresponding psychological effects of donating.

Goal as Defined by the Donor

In addition to the nature of the tie between the donor and the future child, the goal of the act of donating renders UTx, with regard to compensation, more similar to organ donation. As stated, the ultimate goal of UTx is for the recipient to have a child. This ultimate goal, however, is defined by the recipient's experience, not the donor's. The immediate goal of a uterine *donor* is to restore organ function for the recipient. In a kidney, hand, or even heart Tx, restoring functioning for the recipient is the immediate goal of the donor, whether or not he or she is aware of that goal. Many donors probably see their immediate goal as being more closely aligned with the ultimate goal of the procedure. For example, donors might cite their goal as to help a recipient be free from needing dialysis, or to enable a recipient to grip a pen and have improved dexterity, or even simply to help a recipient live. The immediate goal of restoring function cannot be overlooked, however, because none of the ultimate goals can be achieved without accomplishing the immediate goal first. Because compensation affects the experience of the donor rather than the recipient, it is this immediate, even if unobserved, goal of the donor that affects this conversation and recommendation. Therefore, the immediate goal of a uterine donor is comparable to the immediate goal of any other organ donor, is one reason compensation should be considered the same way it would for any other organ donation.

Risks to the Donor

Lastly, the risks incurred by uterine donors are more similar to those incurred by organ donors than to those taken on by surrogates or gamete donors. This is not to say that surrogates and gamete donors do not take on risks. As discussed in the first chapter, surrogates take on the risks associated with IVF and pregnancy, along with the psychological burdens unique to gestating a child that is not biologically theirs. Sperm donors take on a minimal amount of risk in donation because the method by which they donate is not an invasive or particularly burdensome procedure. Egg donors, on the other hand, undergo the risks of a more invasive procedure to harvest the eggs, as well as the burdens of hormone treatment and ovarian stimulation.

Organ donors, however, are subject to the general surgical risks of pain, infection, hernia, bleeding, blood clots, wound complications, adverse reactions to anesthesia, and even death ("Living Donor Transplant"). These risks all apply to uterine donors, because, as previously stated, a uterine transplant is, at its core, an organ transplant. One of the arguments against permitting compensation for organ donors is that it could cause vulnerable populations to take on a considerable amount of unnecessary risk and ultimately be exploited for their organs (Friedman 747). This argument hinges on the risks associated with organ donation generally, which are similar to the risks associated with uterine donation specifically. Therefore, in part because of the risks associated with uterine donation, UTx compensation laws should follow the laws set forth for organ donations.

The main difference between UTx and organ donations is, of course, the ultimate goal of the surgery. As stated, the ultimate goal of UTx is to have a child, not to get an organ; this is clearly illustrated by the fact that the organ is later removed. This difference is also the biggest similarity between UTx and ARTs, which also have the ultimate goal of having a child. However, this similarity between UTx and ARTs is not enough to overpower the similarities mentioned between UTx and other organ donations.

Because of these similarities, as well as the overall similarities between the experiences of organ donors on the whole and uterine donors in particular, compensation laws should follow those for organ donations. This means that payment for a uterine donation or a uterus itself should be illegal (Friedman 746). However, just as is the case with other organ donors, certain expenses of the uterine donor may be covered by the recipient's insurance.

CONCLUSION

Just as in the previous chapter, this discussion of the ethical considerations surrounding UTx donors is far from exhaustive. My recommendations are made given the degree of information available at this time, but many of these matters require continued research. Many of the areas requiring additional research have already been noted, such as psychological effects on the donors and potential differences in pregnancy and birth rates using living versus deceased donors. I touch on them again in the final chapter. There are still other areas of research, such as the potential to create a tissue-engineered

uterus using regenerative medicine, that lie outside the scope of this paper entirely, yet could potentially change the conclusions of this chapter (Atala and Murphy 1413-1414).

While every medical team needs to carefully assess each individual donor, both living and deceased, based on applicable medical, relational, and psychological standards, there must also be an effort to reach a more universal agreement about practice. This consensus must especially be sought with regard to the discussion of living versus deceased donors. By the time UTx moves from research to clinical use, these questions will require uniformity in professional standards to ensure that the ethical considerations are met and applied equally.

CHAPTER FOUR: Remaining Questions & Research Considerations

INTRODUCTION

The purpose of this thesis is to examine many of the major ethical considerations regarding UTx. Specifically, I set out to illustrate and assess several of the ethical considerations regarding UTx recipients and donors using the arguments and frameworks established with ARTs and organ transplants in general. The ethical considerations that I have discussed, however, are far from the only ethical considerations at play. There are many more questions that are outside the scope of this thesis that require further discussion. Some of the questions merit research and discussion immediately because they could potentially affect current research practices. Others are perhaps less immediately pressing, but they warrant discussion before UTx moves from research to the clinic. Still other questions are further off, having to do with ways UTx could be used or issues that could potentially arise once UTx is already being used as a treatment in the clinical setting rather than being limited to the research setting.

This final chapter serves to point out many of these additional questions and ethical considerations. Unlike the previous chapters, this chapter does not necessarily answer these questions, but I hope it will serve as a jumping off point for others to elucidate and expound upon. Finally, and perhaps obviously, the questions and considerations laid out here are far from exhaustive. There are sure to be many other points of research, questions to answer, and ethical considerations to discuss that I have not thought of or that will arise later as the result of ongoing research. The more questions that can be examined before UTx moves from the research phase into treatment, the more likely it is that the medical community will handle the procedure and

those involved in a moral manner. Just as I hope that others will expand upon the topics laid out in this chapter, I hope that my further questions elicit further questions in others regarding UTx and help foster a great deal of dialogue while research oversight entities are still managing the procedure.

ALLOCATION

The issue of allocation was touched upon in both chapters two and three. As with any organ transplant, there is the issue of supply and demand. Regardless of whether only deceased donors are used for UTx or both deceased and living donors are permitted, it is likely that there will be more potential UTx recipients than donors. At the end of 2016, there were 95,456 patients on the waiting list to receive a kidney (Hart et al. 77).[8] Although we do not know the exact number of women who would want to receive a UTx, we can begin estimating based on the number of women affected by UFI and current fecundity rates. Nair et al. illustrate this by pointing out that by 2007 approximately 5,000 hysterectomies were performed per year in the United States in women ages 15-24 due to cancer or benign indications. At the time, the fecundity rate in women of that age group was 85.4%, meaning that approximately 4,000 of that category may have an interest in conceiving (Nair et al. 84-85). Of that group of women, it is unlikely that all 4,000 would want a UTx. Some might consider adoption or surrogacy to satisfy their desire, but many of these women may be interested in pursuing UTx. This number only reflects one category of women affected by UFI. When you consider that in 2008, in the United States alone, over 9.5 million women between the ages of 15 and 44 were probably affected by

[8] We are drawing examples from kidney transplants because it uses both living and deceased donors.

absolute UFI, there is a huge number of women who may be interested in receiving a UTx (Nair et al. 84-85).

Even though we know that it is likely that there will be a shortage of uterine donors, I think it would be useful for research to be conducted to discover a more accurate picture of supply and demand for this procedure. For example, if we were to allow only deceased donors, how short would the supply be? If the research were to show a large discrepancy between supply and demand, I do not believe that this should be used as an argument in favor of using living donors, but I believe that having a better idea of these numbers would help inform discussions about how to handle allocation. Even though the supply and demand may change over time, especially as the procedure begins to be considered more normal, safe, and effective, having more concrete data in this area is still useful. Once the parameters for who is an appropriate candidate to receive UTx are strengthened, a better knowledge of supply and demand would help alleviate speculation regarding what the deficit of uteri would be. Additionally, if there is a large deficit, it may help spur research in adjacent fields, such as the use of regenerative medicine to create uteri to be used in UTx (Atala and Murphy 1413-1414).

Two major questions in the area of uterine allocation are: "Who should handle the allocation?" and "According to what standard is allocation to be done?" The first question follows the question of compensation in the previous chapter. As discussed, in terms of compensation, UTx should be treated like an organ donation rather than like ARTs (i.e. compensation should be prohibited). Similarly, the allocation of uteri should follow the allocation standards currently in place for other organ Tx. Therefore, the Organ Procurement and Transplantation Network (OPTN) should oversee allocation of

uteri, just as they would any other organ, with the United Network for Organ Sharing (UNOS) handling the waiting list.[9] Currently OPTN and UNOS classify uteri as a non-reconstructive VCA, which may render them subject to particular rules when discussing allocation ("List Covered Body Parts Pertaining to Vascularized Composite Allografts" 5). One such regulation that affects allocation is that, as a VCA, uteri donation requires specific authorization, whether by the donor prior to death, or by surrogate decision makers after death ("Guidance to Organ Procurement Programs (OPOs) For Deceased Donor Authorizaton" 1-2). OPTN requires specific authorization for VCAs at the moment because they believe they fall outside what the public has generally understood consent for organ donation to cover. Over time, as the public's understanding of what is included in organ donation changes to include what is now possible with VCAs (e.g. limbs, face, hand, uterus, etc.), I do not believe that uteri should require specific authorization. Unlike other VCAs, a uterine donation does not alter the appearance of the donor, nor does it prohibit a donor from maintaining anonymity ("Guidance to Organ Procurement Programs (OPOs) For Deceased Donor Authorizaton" 3). However, uteri allocation should be subject to the governance of OPTN, which means that until they separate authorization standards for different VCAs, uteri donation will require specific consent.

The second question regarding what standard should be used to allocate uteri is a bit more difficult. As discussed in chapter two, two arguments could be used to help determine how uteri should be distributed: the fair innings argument and the prudential lifespan argument. In general, the fair innings argument would prioritize women closer to

[9] Countries outside the United States should grant oversight of allocation to the entity that oversees all other organ allocation in their country.

the end of their childbearing years, in order to allow them to have a chance at having children during that life stage. The prudential lifespan argument generally tries to ensure that the recipient is getting the most out of the donated organ. In other words it prioritizes younger recipients in order for the organ to be able to have the longest lifespan in the recipient. The prudential lifespan argument falls short with UTx, however, because the recipient does not need to get many years out of the organ, because of ephemeral nature of the procedure and the ultimate removal of the uterus. Because the ultimate purpose of UTx is not to have the transplanted uterus, but rather to have a child, the prudential lifespan argument falls short.

Besides age, there are many other factors that should play into allocation. For example, in chapter two, I discussed that it is in fact acceptable for a woman who is currently a mother to pursue UTx to have another child. That being said, her motherhood status may contribute to where she falls on the organ waiting list. These factors and how they contribute to an allocation score should be examined as OPTN and UNOS take on the waiting list and distribution function for this procedure. As of June 2018, however, the OPTN's policy on VCA allocation only states that the host organ procurement organization (OPO) will allocate VCAs to candidates within their OPO before those outside of their OPO, and within each of those categories, candidates will be sorted and placed on the waiting list by wait time ("Organ Procurement and Transplantation Network Policies" 171). This policy does not discuss any of the other factors mentioned here that might be relevant to uterine allocation. OPTN needs to consider factors such as age, motherhood status, wait time, and status as previous uterine donor to determine a more robust allocation system, perhaps based on points like the Kidney Donor Profile

Index (KDPI) used in kidney allocation. As discussions of allocation continue, medical providers, policy makers, and ethicists need to closely examine the principle of justice to ensure that allocation is being undertaken in an ethical manner.

PAYMENT

As with many novel medical treatments, an underlying issue with UTX, and perhaps the biggest hindrance to it's becoming incorporated into medical treatment, is how much it will cost and who will pay for it. As mentioned previously, my discussion of payments for UTx pertains only to the United States. As healthcare systems and coverage differ from country to country, discussions will be needed as to how UTx should be paid for. As UTx is currently in the research phase, payment now differs from payment for UTx once it is considered a treatment.

According to researchers, the total estimated cost of a uterine transplant is unknown; in various interviews with researchers they have estimated the cost of the procedure alone has differed and has been quoted as anywhere from $150,000-$500,000, to $200,000, to $250,000 (Sifferlin, "4 Breakthrough Uterus Transplants; Jochem). These discrepancies in estimates illustrate just how much is unknown about the costs of this procedure. While UTx is still experimental, research funds cover the procedures, but research criteria are careful to note that recipients: "Must have the ability to fund, either through third party coverage or through other their own personal financing, any expenses associated with assisted reproduction services provided to them" ("Uterine Transplantion and Pregnancy Induction in Women Affected by Absolute Uterine Infertility"). Even in the experimental phase, therefore, this limits recipients to those who can afford the anticipated costs

associated with IVF. IVF is estimated as costing as much as $17,000 per cycle and often requires multiple cycles to achieve pregnancy (Bayefsky and Berkman 361). Although ART is sometimes covered by insurance plans, it is not uncommon for recipients to have to pay for their treatment out of pocket. Additionally, it is unclear if insurance currently covers the costs of the immunosuppressants needed following this experimental surgery, or if that associated cost is also an out of pocket expense for the recipient.

When UTx is no longer in the research phase, recipients of UTx will have to pay out of pocket or rely on third party coverage. Just as with compensation to uterus donors, a discussion of payment and coverage must begin by determining if we are classifying UTx as an ART or an organ transplant. When considering compensation, I classified UTx as an organ donation because that best characterizes the donor's experience. With payment for UTx, however, we must look at the nature of the procedure as defined by the *recipient's* experience, given that payment affects the recipient but has no bearing on the donor. That being said, the nature of this procedure is defined by the recipient's ultimate goal of having a child, not just restoring organ function. Therefore, for the recipient, UTx is a form of ART that happens to involve an organ transplant. For this reason, in the case of payment, I argue that we must rely on the discussions of payment for ARTs.

In the United States, ARTs, such as IVF and surrogacy, are often excluded from medical coverage ("Uterus Transplants Raise Hope and Questions"). It is likely that UTx would be similarly excluded. Given that it is an expensive procedure, it would be limited to a small group of women who could pay for it. A discussion of whether this is ethically acceptable extends beyond this paper and beyond UTx on its own. There are many

questions that need to be discussed about payments/coverage for all infertility treatments, which can then be applied to UTx as a treatment.

The first question to begin these discussions is whether humans have a positive right to reproduction (i.e. a right to receive treatments to achieve reproduction) or only have a negative right to reproduction (i.e. a right to not have their ability to reproduce inhibited, through things such as forced sterilization, etc.)? If there is a positive right to reproduction, then several more questions arise. The first would be, who has the duty to uphold this right (government, insurance, etc.). Second, if there is a positive right to reproduce, to what extent does this right exist? Last, when is the obligation to uphold that right fulfilled? For example, could the state be obligated to provided as many cycles of IVF as it takes for a woman to become pregnant, or might the state's obligation be fulfilled after three cycles of IVF, even if unsuccessful? Could a positive right extend to having multiple children, or is the obligation fulfilled if an individual or couple has a single child?

I agree with John Robertson's argument, in which he states that procreation is a fundamental human right, yet the obligation to uphold this right is fulfilled as long as individuals are not prohibited from having genetic children using safe and effective technologies (Robertson, "Other women's wombs" 69). He further emphasizes this point in stating that reproductive rights are "rights *against the state* limiting or restricting an individual's reproductive choices or efforts to obtain reproductive services form a willing provider. They are not rights to *have the state provide* the services or resources needed" (Roberston, "Harm to offspring in assisted reproduction" 20). Robertson therefore states that if UTx is proven to be safe and effective, the state should not impose restrictions on

who can receive UTx (Robertson, "Other women's wombs" 85-86). As a negative right against the state, UTx would not be required to be provided by the state, and presumably would not be required to be covered by insurance.

In order to more fully discuss payment and potential coverage by insurance, we must examine whether infertility is a disease state. In a study of public attitudes in the United States regarding insurance coverage for IVF, researchers found that those who considered infertility a disease largely felt that insurance should cover fertility treatments (Ho et al. e9). That same study, however, found that most Americans did not consider infertility a disease (Ho et al. e9). Furthermore, if we say that infertility *is* a disease, then it bears discussing whether *all* reasons for the inability to reproduce are considered diseases or whether just certain reasons for this inability are disease states. For example, if a woman is born with Mayer-Rokitansky-Kuster-Hauser syndrome and thus does not have a uterus, that infertility may be a disease. On the other hand, what if a woman is 48 years old, beyond "normal childbearing years," and is unable to become pregnant? Is that type of inability to reproduce also a disease? It seems unfounded to conclude that *all* inability to reproduce is a disease state, but where and how should the lines be drawn when determining which types of infertility are diseases? This discussion needs to be unpacked further in order to determine whether insurers should be required or encouraged to cover infertility treatments.

FURTHER RESEARCH

Many of the questions that remain to be discussed and answered require additional research. While much research has been conducted to get UTx to where it is

today, there is much more research to be done. Below are a number of research questions that arose in examining the ethical considerations of UTx recipients and donors. I do not delve into the specific methods of research, but merely point out that answers to these questions are imperative as UTx moves from research to treatment. This future research should be overseen and compiled by the International Society of Uterus Transplantation (ISUTx) so that the field can learn and advance in a consistent and ethical manner. I have divided these questions into the quantitative and qualitative categories for clarity of discussion.

QUANTITATIVE

One of the major questions I address is the use of living versus deceased uterine donors. I argue that the use of living donors is impermissible unless research with LDs shows significantly greater success than with DDs, with success defined not by graft survival, but by pregnancy and live birth rates, and shows that the risks to LDs are acceptable. I think this is one of the largest areas of research to be done with UTx. In order to begin a comparative study of this sort, it may be useful to begin with animal models. A study of this sort would allow researchers to determine what, if any, benefit there may be in using living uterine donors. If the research shows that using LDs increases the pregnancy and live birth rates in the animals, then a comparative study of this sort in humans can be discussed. Until research shows that LDs increase the likelihood of success of the procedure, as defined by pregnancy and live birth rates, all future UTx research in humans should use DDs.

Another study that may prove useful in the discussion of living versus deceased uterine donors is a study of the effects of ischemic time on the uterus. Studies in other transplants show that greater ischemic time can cause systemic inflammation and higher risk of graft failure (Kisu et al. 1407). More research should be done on the length of ischemic time that a uterus can withstand. Knowing this time is especially important if we move toward using only DDs. Organ procurement from DDs is often more difficult because you cannot plan for it in the same way you can plan for removing an organ from a living donor (Lavoué et al. 272). This lack of planning often contributes to a longer ischemic time for the harvested organs (Kisu et al. 1407). In 2017 a new protocol was released for retrieving uteri from deceased donors to mitigate these issues seen in DDUTx. According to this protocol, the uterus can be removed prior to the procurement of other organs without increasing their ischemic time (Testa et al., "Deceased donor uterus retrieval" 680). This retrieval can be performed prior to subsequent organ procurements because it can be completed prior to the cross-clamp, which allows blood to still reach the organs. Because the other organ retrieval teams are not yet present, the uterus retrieval functions in the same way as it would in a LDUTx. This protocol is modeled on a liver split technique that similarly occurs before cross-clamp and the presence of other retrieval teams (Testa et al., "Deceased donor uterus retrieval" 680). This protocol greatly reduces the ischemic time of the uterus, without increasing the ischemic time of other organs, and allows the team to easily retrieve the desired vascular anatomy for the UTx. This new protocol is a great example of the way researchers can help develop more efficient protocols to effectively procure uteri. Even though this technique mitigates the problem of ischemic time of the uterus, it is still an area that I

believe requires more research because ischemic time can never be fully eliminated. Therefore, in addition to knowing the ischemia that a uterus can withstand, it is important to discover what the effects of different ischemic times are on pregnancies, births, and future children.

Other quantitative questions pertain not to the surgery itself, but to the aftermath of the surgery. Following the Tx, the woman undergoes IVF in order to conceive. Although we have data on IVF in general, there is very little information about IVF in UTx recipients specifically. In 2012, the CDC found that for women under the age of 35 undergoing IVF, only 46.6% of cycles resulted in pregnancy and only 40.5% of cycles resulted in a live birth ("2012 Assisted Reproductive Technology"). Currently, it is assumed that the success/failure rate will be the same in women with their own uteri and those with transplanted uteri; however, this is not an area that has been studied. The failure rate is important to help give clinicians and patients a better understanding of what to expect when undergoing this procedure.

Another piece of the UTx protocol is that following one to two births achieved via IVF and C-section, the transplanted uterus is removed. At the moment however, we have very little information on a subsequent UTx conception and pregnancy. As of this paper, only one of the recipients has birthed more than one baby and there is very little research regarding this aspect (Gustafsson Kubista; Del Priore 290). Del Priore recommends using animal models to study whether there may be any unanticipated consequences for a second pregnancy and birth following UTx (Del Priore 290). In addition to this research, providers should proceed with caution in UTx recipients undergoing their second pregnancy. Their progress and outcomes should be monitored carefully and any

abnormalities should be noted. If there are unanticipated consequences with a second pregnancy, this may affect the standard UTx protocol.

One broad question bearing research is whether there are any potential risks to the future children. Upon hearing this question, most immediately think of the effect of immunosuppressants during pregnancy. The risk of immunosuppressants during pregnancy does not worry researchers, however, because immunosuppressants have been used during pregnancies for many other organ transplant recipients. That being said, the actual data we have on this subject are limited (Fuchs and Coustan 363). This is a topic across the transplant community that bears more research in order to know exactly what the risk is of immunosuppressant use during pregnancy. If there are any risks to the future child due to immunosuppressant use during pregnancy, they may ethically be incurred for mothers who received a life-saving transplant. Those same risks, however, might not be incurred ethically in a UTx recipient, as the procedure is not life-saving (Caplan at al. 19). That being said, protocols for other quality of life transplants, such as face and limb transplants, do not advise against getting childbearing due to risk of immunosuppressant use during pregnancy, so it is unlikely that this argument would apply to UTx.

Additionally, immunosuppressants are not the only thing that may affect the future child. As mentioned in the previous chapter, thrombosis is one of the greatest risks following UTx. Thrombosis in pregnancy could inhibit fetal development, cause fetal death, induce preterm delivery, and cause developmental problems associated with poor circulation, infection and loss of fluid (Caplan et al. 19). Although we understand these risks to an extent, research should be done to assess the degree to which these risks may affect a pregnancy and the future child and how they can be minimized.

QUALITATIVE

In addition to the quantitative studies that need to be conducted, there are many qualitative studies the results of which may affect how UTx should be pursued. Arora and Blake suggest that one area that needs to be investigated is the extent to which UTx improves the quality of life of a woman with UFI over surrogacy or adoption (Arora and Blake 398). Their reasoning for this study is to determine the actual benefit of UTx. Many women express their desire to pursue UTx to experience gestation of their child; however, can we determine if this experience actually does lead to better quality of life for the recipient than does the experience of surrogacy or adoption? If this study were to show that UTx actually did not produce a better quality of life than these alternatives, does that mean that it is not a worthwhile treatment to pursue?

Another qualitative area of study necessary is the psychological effects on both recipients and donors (if living). Given that I discuss psychological effects in both chapters two and three, I do not need to fully delve into why the psychological effects are important and why additional research is needed (Järvholm et al). Briefly, several of the areas of psychological effects that should be examined further are: 1) the psychological effects following related vs. unrelated (living) UTx donors, 2) the psychological effects following identified vs. unidentified (living) UTx donors, 3) how psychological effects differ for the UTx recipient vs. women receiving other ARTs, 4) the psychological effects of graft failure for both the recipient and the (living) donor, and 5) general psychological follow-up to assess psychological risks such as depression, suicidality, etc. in both the recipient and the (living) donor. Understanding these potential psychological risks will

help medical teams and psychologists develop tools to help these donors and recipients. As of now, researchers are using "'borrowed' psychological tools from transplant centers, adoption agencies and ART centers" (Del Priore 290). While these borrowed tools are helpful, we need to know more about the particulars of what these women are facing. Just as I have discussed throughout this thesis, UTx is a unique mix of ART and organ transplants. At this intersection, there are certain psychological effects to expect from each of those areas; however, the intersection also means that there is an interplay of the effects from both ARTs and organ transplants that cannot be adequately anticipated without further study.

Medicine as a field must always be open to further research. These research topics are some that occur to me now as being necessary or helpful. It is important to note, however, that the more research is done, the greater likelihood there is that more areas needing research will come to light. As always, providers, ethicists, and researchers themselves must be aware of these areas and willing to use research to influence current standards of practice.

FURTHER ETHICAL DISCUSSIONS

The aforementioned topics are some of the more obvious questions that arise when discussing the future of UTx. These, however, are far from the only questions that may come up as UTx progresses. Even more so than in the first half of the chapter, in this

half I will not provide answers or even strong opinions, instead, this half is meant to bring questions and potential issues to the surface and invite others to discuss and answer.

PRONATALISM

One of these questions is, "Does UTx promote and enable a pronatalistic society?" I touched on this issue in the second chapter when assessing women's reasons for pursuing UTx. In that chapter, I conclude that even if UTx does indulge the pronatalistic tendencies of our society, this should not prohibit it's pursuit by those who desire to use it to have a child. That being said, if UTx does become a treatment, we must carefully consider the role it plays in promoting pronatalism and try to address the root of the issue. According to Bartholet, pronatalism is characterized by "glorifying procreation and childbirth, while at the same time stigmatizing infertility and adoption" (Bartholet 9). Perhaps combatting this societal issue will require changes to adoption restrictions or employer benefit packages covering infertility treatments and adoption. Maybe the answer is a bit more abstract and involves changing the way society speaks about having children or choosing not to. Even though these questions are not unique to or caused by UTx, they are inextricably linked to this conversation and bear further discussion.

Another question involving the pronatalism of society is, "How do we determine the appropriate number of pregnancies or births after the transplanted uterus should be removed?" Currently, the suggestion is that after one or two births, the uterus should be removed to avoid long-term use of immunosuppressants. Although the reasoning for this stems from the principle of nonmaleficence, minimizing the risks for the uterus recipient, how this number fits society's conception of a "correct" family is a matter of concern. If

a woman or couple wishes to have a larger family and does not want to stop after two children, can a medical team require the removal of the uterus in order to protect the woman from the risks associated with immunosuppressants? Furthermore, I wonder if the decision to remove uterus after two births stems from medical reasons (e.g. the length of time after which the risks of using immunosuppressants rises) or because this fits in with the conception of a "normal" family (as of 2017, the average number of children in a family, according to the United States Census Bureau is 2.54). Just as research should be done on the effects of a second pregnancy and birth following UTx, perhaps more research should be done to determine if more than two births can be achieved safely.

On the other hand, if a woman or couple wants a smaller family and therefore wants to remove the transplanted uterus after only one child, this is certainly not prohibited. However, I wonder if the emphasis on having two children, and therefore playing into the idea of a "normal" family, would create pressure to have another child. Perhaps the parties involved (recipient, donor, OPTN) may also feel as though the transplant was wasted if the recipient does not have two children from it. Again, addressing these issues involves changing discussions of what constitutes a normal or good family. Pronatalisim is not an issue for UTx alone; however, those that are involved in UTx should be involved in addressing the associated issues, as they may arise or deepen as UTx moves toward becoming a treatment.

CLAIMS TO PARENTHOOD

One issue that may arise as UTx becomes a treatment is the potential that a uterine donor will claim a right to parenthood (Öztürk 82). Given that there have been

examples of claims to motherhood from both surrogates and gamete donors, it seems unlikely that this would not ever become a question with UTx. Even if one thinks this is a ludicrous claim, it is a question that needs to be addressed. There are obviously differences between a uterine donor and a surrogate or gamete donor; namely, uterine donors are neither gestating the child nor are they genetically related to the future child (unless that familial connection occurs outside the transplant, such as a mother donating her uterus to her daughter). That being said, there is still a degree of connection between the two individuals, and it is not hard to imagine some kind of epigenetic claim. In a 2013 Irish surrogacy case, experts argued that the surrogate had a parental claim to the child because of the role of epigenetics. They argued that the environment created by the surrogate's womb interacts with the underlying genetic makeup of the child, which contributes to which genes are expressed, which can potentially influence the development, outcomes, and specific characteristics of the child (Christiansen 319-320). Although a surrogate has more control than a UTx donor over the environment created by her during pregnancy through things like diet, supplements, lifestyle choices, and exercise, the uterus itself contributes to the environment created for the fetus. Because of this environment and its role in genetic expression, it is not unlikely that a UTx donor could claim an epigenetic relationship to the future child whose birth is achieved by UTx.

This claim to parenthood, or more mildly, a claim to a right to have some sort of relationship with the child, could apply to both LDUTx or a DDUTx. If an unrelated LD were used, would she desire to meet the future child? If she changed her mind regarding ceasing having children or regretted her decision to donate, would she have any basis to

claim a right to parenthood? This is a question for ethicists as well as legal scholars to address if and when the issue arises in the courts.

Even if a DD is used, could the remaining family of the donor claim any parental rights or right to a relationship with the child? Although one might dismiss this question due to the fact that it is just an organ, there is plenty of anecdotal evidence of family members feeling emotional ties to the recipients of their loved one's organs. There are many stories in the news of fathers, mothers, husbands, and wives meeting the recipients and feeling either a connection to their deceased loved ones or closure about their death (Earl; Flam). As heartwarming as these anecdotes of these meetings are, what if the recipient does not wish to reciprocate? This connection and desire for a relationship may get trickier when there is a new life involved. The deceased loved one has not only helped another's life, but has contributed to creating a child. Given this, what sort of perceived connection might the DD's family have to the child? What if they feel they have a parental right given that their loved one's *organ* was involved in gestating the child? Legal scholars need to begin addressing these questions and helping to establish legal frameworks and protocols to eliminate or minimize the potential for these issues.

MATERNAL FETAL CONFLICT

Caplan et al. raises the issue of the risk of organ failure. If the organ fails, it can simply be removed. Because UTx is not a life-saving procedure and the uterus is a non-vital organ, its removal if the graft fails is not terrible. However, as Caplan et al. raise, what if the graft failure occurs while there is a fetus in the womb (Caplan et al. 19)? This question is not unique to UTx. Issues of maternal fetal conflict can arise in any pregnancy

(Oberman). In other pregnancies, this may involve issues of whether a provider can compel a woman to receive a particular type of treatment to save herself, even if it may hurt or even abort the baby. This issue does not differ materially from the question of organ failure in UTx. The application of reproductive ethics concepts to UTx is still a discussion worth having before the issue arises.

EXPANDING UTX RECIPIENTS

In chapter two, I addressed some of the ethical considerations surrounding UTx recipients. Those considerations, however, are far from exhaustive and were restricted to the current state of UTx. As UTx moves from research to treatment and eventually becomes more normalized, it is likely that expansions of categories of recipients will be proposed. Below are three potential extensions that I briefly address to invite future discussion.

Former UTx Donor

If a woman has acted as a UTx donor, has she eliminated herself from potentially receiving a donated uterus in the future? Or should that same donor-turned-recipient receive higher priority in receiving a UTx? For example, what if the woman donated her uterus when she was single and earnestly felt as though she did not desire to have children, and therefore donated her uterus to her sister who desired children but had UFI. What if many years later she is now married and has changed her mind regarding having children? Does she have to simply live with her previous decision and pursue surrogacy or adoption? Or is she eligible to receive a UTx? If she is eligible to receive a UTx,

should she receive priority given her previous role as a UTx donor? This model of prioritization of previous donors currently exists within kidney Tx allocation. Those waiting on a kidney who have previously served as a living organ donor get "points" added toward their KDPI, which is used to rank potential Tx recipients and determine an allocation waiting list (Israni et al. 1844). Should this model be applied to Utx? Prioritizing women who have served as UTx donors might help expand the donor pool by helping decrease the fear of having a change of heart regarding having more children.

To Have a Non-Genetically Related Child

Currently, UTx is restricted to use with the transplant recipient's own eggs. This means that if a woman has already undergone menopause or has undergone treatment that has affected her ovaries (e.g. chemotherapy and radiation) and has not previously frozen her eggs, UTx is not an option for her. As UTx progresses, however, it is very likely that women, or genetic males as we will see in the next section, will want to use UTx in conjunction with gamete donation. Are there ethical reasons why this differs from using UTx with one's own eggs? There is no medical reason why using donated eggs is problematic; therefore, an argument against this expansion would have to be made on a moral basis.

Non-Genetic Female

The first point in the first section of the Montreal Criteria requires that the UTx recipient is a genetic female (Lefkowitz et al., "An Update of the Montreal Criteria" 924). This limits the procedure from being used by males or trans individuals hoping to gestate

a child. As mentioned in chapter two, the reason for this restriction is that animal and human trials have only dealt with genetic females to date. Furthermore, transplanting a uterus into a non-genetic female has many additional surgical and medical requirements, including "the creation of adequate uterine vascularization de novo, the necessity for appropriate hormone replacement to sustain implantation and pregnancy, and the placement of the uterus in a nongynecoid pelvis" (Lefkowitz et al., "An Update of the Montreal Criteria" 924). Given these medical complications and the lack of research, the procedure should remain limited to genetic females at present. However, Lefkowitz et al. state that they do not believe it is unethical for a non-genetic female to receive a UTx.

There are two major arms of the discussion that need to be handled in order to expand the use of UTx to non-genetic females. The first is whether using UTx for non-genetic females is an appropriate endeavor. This discussion will involve questions of what the role of medicine is, who has a right to reproduce and gestate, and what type of right it is (negative right, positive right, etc.). If that discussion concludes that it would be an appropriate endeavor for a non-genetic female to pursue UTx, there would be a great deal of research required before UTx should be attempted in non-genetic females. This research would obviously first begin with animal studies before progressing to ethical human research on the subject.

Even as I write these questions, many of these issues come across, even to me, as either extremely pessimistic or fodder for science fiction. However, my hope in raising these questions is that discussions can be held before the issues are actually brought into

reality. Although conclusions may not be reached, especially those that may establish a legal precedent (e.g. maternal fetal conflict, parental claims, etc.), the sooner varying perspectives and arguments are brought to light, the easier it will be for UTx to transition to treatment and remain in the good graces of society.

CONCLUSION

Bioethics is an ever-evolving field that adapts and responds to new technologies and to an ever-changing society. UTx is one such technology that is changing the landscape of infertility treatments. There are many questions that still need to be addressed and many questions that will arise as research continues on UTx. This thesis provides an overview of the landscape of the discussion and insight into some of the biggest conversations surrounding the procedure. While UTx provides hope for many women faced with UFI, researchers, medical teams, and ethicists must ensure that the manner in which UTx is experienced for recipients, donors, and society as a whole is ethical. The more conversations that can be had and conclusions that can be reached while UTx is still experimental, the better equipped the medical community as a whole will be to act ethically in using this novel procedure as a treatment.

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