The Ethics of Uterine Transplants: A Revolutionary Treatment for Women with Uterine Factor Infertility

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Abstract

Uterine transplantations are a groundbreaking procedure for women with uterine factor infertility (UFI). Through this procedure, women with UFI are able to carry and deliver their own biological children with the implementation of a live or dead donor uterus. With the recent birth of a baby from a dead donor uterus in Penn Medicine's UNTIL trial, uterine transplantations are being considered as a viable third option for women with UFI. Traditionally, women with UFI have only had the option of adoption or in-vitro-fertilization (IVF) using a gestational carrier. Despite the rapid advances in the development of uterine transplantations, the ethical issues surrounding this novel procedure have been vaguely addressed. In this paper, we will analyze the ethical concerns surrounding uterine transplantations, which includes a consideration of emotional, physical, psychological, and financial factors. With an understanding of these ethical concerns, we will make an argument for the use of uterine transplantations for women with UFI. Recommendations for the selection of donors and recipients for uterine transplantations will also be provided.

INTRODUCTION:

As scientific research on reproduction has progressed, assisted reproductive procedures have become increasingly prevalent. In the last two decades, the use of assisted reproductive services have increased approximately 13 % to 16 %.[1] Since its emergence in Saudi Arabia in 2000, uterine transplantation has been a groundbreaking surgical procedure to help women who have uterine factor infertility (UFI). According to Penn Medicine, it is estimated that approximately 5 % of reproductive age women worldwide are affected by UFI.[2] Women with UFI are unable to become pregnant due to the presence of uterine abnormalities, and UFI has traditionally been considered incurable. When diagnosing UFI, some women have a congenital abnormality, while others develop acquired abnormalities from surgery or a past infection.[3] Congenital abnormalities of the uterus for women with UFI typically include a failure of the uterus to form, duplication of the uterus, two uteri sharing the same cervix and vagina, a fibrous band down the center of the uterus, and a dent in an otherwise normal uterus.[4] Unlike congenital abnormalities, acquired abnormalities include the growth of noncancerous uterine fibroids that distort the endometrial cavity, infection of the endometrium, scarring of uterine tissue, and the endometrium breaking through the myometrium.[4] A hysterectomy is typically conducted to treat some acquired abnormalities, which leaves women infertile due to the removal of the uterus.

Through the presence of acquired or congenital abnormalities, women with UFI have had few options for having children. Traditionally, the utilization of in-vitro fertilization (IVF) with a gestational carrier and adoption have been the only two options available for infertile women who desire to raise children.[5] However, uterine transplantations have the potential to be a viable third option for women with UFI that allows them to carry and deliver their own babies. In order to deliver their own babies, women with UFI have traditionally received uteruses from live donors. In 2000, the first reported human uterine transplantation occurred in Saudi Arabia, and involved the use of a live donor.[6] The live donor was a 46-year-old woman with multiloculated ovarian cysts who agreed to donate her normal uterus after having a hysterectomy, while the recipient was a 26-year-old woman who had acquired UFI six years earlier through enduring a postpartum hemorrhage after a Cesarean section, which resulted in a hysterectomy.[7] Even though the uterus was successfully

transplanted into the recipient, the uterus had to be removed through a hysterectomy after 99 days, as blood flow to the uterus eventually failed with the development of acute vascular thrombosis in the recipient.[7]

Despite this initial failure to produce a viable offspring, researchers in Sweden eventually reported the first live birth from a uterus transplant in 2014. The donor was a 61-year-old woman with two children who donated her uterus to a 35-year-old recipient with UFI who lacked a uterus.[8] The successful production of an offspring with uterine transplantation from a live donor indicated that this procedure was feasible, even with a uterus from a postmenopausal woman. However, the baby was born premature by approximately two months with a normal birthweight for gestational age, which indicates a potential complications for this procedure.[8] Complications with live donor uterine transplants have continued in the United States. For example, in November 2017, the first baby from a uterine transplantation with a live donor was born in the United States at Baylor University Medical Center.[9] Despite this success, four of the first eight women in Baylor's clinical trial who received a uterus from a live donor had to have their uterus removed due to complications from organ rejection.[10]

Instead of using live donors, researchers have begun using uteruses from deceased donors. Potential advantages of using deceased donors include eliminating surgical risks to live donors, and the ability to harvest more blood vessels from the organ as compared to a live donor organ.[11] In addition, dead-donor uterine transplantation can increase the supply of organs, and allow more patients access to the procedure.[12] In 2016, the first dead donor uterine transplant was performed at the Cleveland Clinic, but the uterus was removed 12 days after surgery due to life-threatening complications from a Candida albicans fungal infection.[12] The recipient was believed to have developed the infection after receiving a uterus from a dead donor with a Candida albicans infection in her bladder, which researchers were not aware of.[13] Even though organs are tested for infections before transplantation, the lack of a national registry for organs can lead to breakdowns in communication. After the failure of the procedure, critics of the procedure were outraged at a perceived lack of accountability in the U.S. transplant system that undermined patient safety.[13]

In the summer of 2019, the Cleveland Clinic reported the first successful live birth from a patient that was transplanted with a deceased donor's uterus in the United States.[12] The recipient was successfully impregnated through IVF in late 2018, and the baby was delivered through a Cesarean section.[12] Recently, in March 2020, the Cleveland Clinic delivered a second baby through a uterus transplantation using a deceased donor uterus.[14] To date, the Cleveland Clinic has performed eight uterus transplantations using dead donors, with six successful transplantations and two transplantations resulting in hysterectomies for undisclosed reasons.[14] Furthermore, in November 2019, researchers at Penn Medicine reported the second ever birth of a child from a patient that was transplanted with a deceased donor's uterus.[15] The case study of this experience will be described in this paper.

Even though recent uterine transplants have been successful, the ethics of uterine transplants have been vaguely addressed. The goal of this paper is to examine the ethics surrounding uterine transplants and propose ethical guidelines for medical professionals. For example, the physical, psychological, and emotional impact on recipients, donors, and developing offspring will first be discussed. Since uterine transplantations are considered to be a nonessential and temporary procedure, the financial costs of the procedure will also be analyzed. In addition, the medical technicalities of uterine transplants will be analyzed. After discussing the medical and ethical considerations of uterine transplants, an argument will be made in favor of the use of uterine transplants.

CASE STUDY:

A thirty-three year old woman named Jennifer Gobrecht (JG) is a Philadelphia native that suffers from a congenital condition known as Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome.[15] MRKH syndrome is a rare disorder that affects the reproductive system of women, and is characterized by the failure of the uterus and vagina to properly develop before birth.[16] Approximately 1 in 4,000 to 5,000 women suffer from MRKH in the general population.[16] Despite the lack of function or absence of the uterus, the presence of normal genitalia and ovarian functions is typically observed in women with MRKH.[16] Even though JG lacked a uterus since birth, she was not diagnosed with MRKH until she was 17 years old.[15] The presence of a delayed diagnosis is a common feature of women suffering from MRKH. The average age for the diagnosis of MRKH falls between 15 and 18 years old, and the key indicator for diagnosing MRKH is the lack of formation of a menstrual period in adolescent females.[17] After learning of her inability

to carry her own child, JG was emotionally distraught. JG was devastated by having the dream of growing a baby in her womb and the dream of feeling her baby kick getting taken away, as she longed to be a loving mother.18 Without a cure for her infertility, JG was left with the limited options of adoption or the utilization of IVF with a gestational carrier.

Between these two options, JG decided to explore IVF. JG and her husband decided to undergo IVF, and had the resulting embryos frozen as they looked for a gestational carrier.[15] While looking for a carrier, JG decided to join Penn Medicine's new Uterus Transplantation for Uterine Factor Infertility (UNTIL) trial in 2017.[15] JG eventually received a dead donor's uterus from the Gift of Life Donor Program, and underwent a 10-hour uterus transplant procedure.[15] After the transplantation, JG had to follow a challenging regime, and was given standard immunosuppressant medication to prevent her new organ from being rejected from her body's immune system.[11] Six months after the successful uterine transplantation, JG was implanted with a cryopreserved embryo from her previous IVF procedure.[15] Surprisingly, JG was able to become pregnant with her foreign uterus.

After becoming pregnant, JG delivered a healthy baby boy at the Hospital of the University of Pennsylvania via cesarean section in November 2018. Babies from uterine transplantations are typically delivered by cesarean section, as women with UFI lack a normal vaginal canal.[19] Since uterine transplantations are a temporary procedure, JG had her uterus removed via a hysterectomy following the procedure. After removing the uterus, JG was able to be taken off the anti-rejection medication she was receiving.[19] JG's successful uterine transplantation with a uterus from a dead donor shows the potential for uterine transplantations to be a viable third option for women with UFI who desire to have children. Even though uterine transplantations are currently only available in clinical trials, they can provide women like JG with a realistic feeling of motherhood through being able to carry and deliver their own children.

MEDICAL ANALYSIS:

In the United States, infertility is a relatively common issue for women. According to the Centers for Disease Control and Protection (CDC), about 6.1 million women in the United States between the ages of 15-44 struggle with becoming pregnant or staying pregnant.[20] Without being able to become pregnant, women with UFI suffer tremendous emotional burdens. For example, the mental health of women is negatively influenced by the presence of UFI. Women with UFI often suffer from a range of mental health disorders with anxiety and depression being the most commonly reported mental health concerns.[21] The anxiety and depression felt by some patients with UFI is considered to be an emotional burden comparable to individuals with more life-threatening conditions. According to a study of 488 American women, women with infertility felt as depressed or anxious as individuals who had diseases such as cancer and conditions like hypertension.[22]

Along with anxiety and depression, the relationships of women suffering from UFI can be detrimentally impacted. In some instances, couples dealing with infertility issues may avoid social interaction with families who have children, and distance themselves from friends who are pregnant.[22] This practice of social avoidance can be explained by the heightened levels of anxiety and stress infertile women feel when encountering external stimuli that remind them of their inability to conceive. Furthermore, the primary relationship with a spouse or partner can be strained through the frustration of intercourse. Since intercourse often allows couples to emotionally connect, having intercourse be associated with the failure to procreate can cause severe conflicts between partners.[21]

For women with UFI, uterine transplants are seen as a viable way to escape the emotional burdens associated with infertility. Being able to raise their own children in their own womb, women feel a sense of empowerment and confidence in their ability to manage the challenges of motherhood.[23] Uterine transplants are currently the only way for women with UFI to become pregnant, and have the emotional experience of raising a child in their womb. However, the short-term and long-term effects on the recipients, donors, and offspring involved in uterine transplants must be critically analyzed.

Impact of Uterine Transplantations on Donors

In terms of short-term effects, the complexity and length of the donor procedure poses a physical risk to the women. One of the main challenges with live donor surgery is the proper extraction of uterine veins. In donor preoperative images, uterine veins are often difficult to see, and the number and diameter of these blood vessels are inconsistent.[24] Along with the lack of image clarity, the procedure of extracting veins is extremely tedious. In the removal of the uterus from the donor, meticulous dissection of the uterine veins and uterine arteries is required to separate these blood vessels

from a strong attachment to ureters.[25] This separation typically involves severing numerous major vascular branches, and allows for an eventual separation of the two arterial and venous vascular pedicles from the uterus.[25] Even though this procedure is done by a large team of experts, the procedure is extremely time consuming. A uterine transplantation donor procedure takes between 10-13 hours due to the challenges involved with removing the veins.[25]

Due to the extended length and complexity of the procedure, donors are exposed to a higher chance of complications. As of 2018, 14 % of live donors suffered ureteral injuries due to the procedure, which is a much higher complication rate when compared to the 0.1 % - 0.5 % complication rate of a simple abdominal hysterectomy.[26] In terms of complications in donors, the first live uterine transplant cases in Saudi Arabia involved a minor complication during surgery. The donor experienced an intraoperative small laceration of the uterine wall; however, this complication was able to be easily stitched up during the surgery.[27] In addition, another donor complication occurred in the 2014 Swedish trials after the donor's uterus was removed. On day 16 after the procedure, the donor experienced a ureterovaginal fistula characterized by the presence of watery vaginal discharge.[25] This complication was promptly addressed through the insertion of a pyelostomy catheter, and the donor's ureter was reimplanted 118 days later with no further complications being reported.[25] To date, there have been no reports of any donor casualties involving uterine transplantations.

Along with short-term impacts, live donors can also experience many long-term impacts of uterine transplants. For example, the extended amount of time under anesthesia could pose severe complications for donors. Administration of general anesthesia for the duration of more than 6 hours is related to an increase in the presence of perioperative complications and mortality.[28] Even though general anesthesia is considered to be fairly safe, some long-term impacts of anesthesia include nerve damage and cognitive dysfunction.[29] In addition, donors can face long-term emotional consequences based on the results of the recipient. For organ donations in general, some studies have suggested that recipient death or graft failure was related to the presence of regret of donation and a lower quality of life.[30] On the other hand, a successful recipient outcome was correlated with a decrease in depression index scores in donors after 19 months.[30]

Even though the surgical complications to live donors are relatively low, dead donors have started to become used in place of live donors. Dead donors are individuals who have passed away from accidents or medical conditions, and have had their family or next of kin agree to donate their organs.[2] Through utilizing dead donors, there is a tremendous benefit of having no donor risk for surgeries.[31] Along with the benefit of no donor risk, the overall surgical dissection time is shorter, and larger diameter blood vessels can be used to simplify the uterine transplantation procedure.[31] The use of dead donors also presents the opportunity to increase the supply of uteruses for women undergoing uterine transplantations, which could make this procedure more accessible in the future.[12] The utilization of the dead donor uterus would have to be approved by the respective next of kin, and the uterus is typically harvested after more critical organs, such as the heart.[32] Despite the presence of enormous benefits for dead donor transplantations, there are also some risks. For example, the ischemic time is generally longer in a deceased donor's uterus than a living donor, which could result in an increase of postoperative rejection.[31] Evidently, both deceased donors and living donors have pros and cons in the context of uterine transplants; however, dead donors appear to be more impactful.

Impact of Uterine Transplantations on Recipients

Uterine transplantations also have several short-term and long-term influences on the life of a recipient. Similar to the procedure for donors, the procedure for recipients is extremely lengthy. The Cleveland Clinic estimates that uterine transplantations take between 6-8 hours.[12] The transplantation time could be closer to 10 hours for recipients when considering the length of JG's procedure in Penn Medicine's UNTIL trial. In order to reduce both of the recipient and donor surgical times, robotic-assisted uterine transplantation has been utilized in previous uterine transplantations. In a trial using robotic-assisted uterine transplantation, the donor's surgery was only 6 hours long, while the recipient's surgery was nearly 9 hours long.[33] With the use of techniques to lower surgery time, both the donor and recipient have the potential to avoid perioperative complications and serious side effects of lengthy exposure to general anesthesia.

Since achieving venous flow is one of the greatest challenges of uterine transplantation, it is understandable why the procedure is so lengthy.[24] In the recipient's procedure, the donor's uterus must be carefully transplanted

into the recipient, and blood vessels must be reconnected to produce adequate blood flow throughout the uterus.[34] A potential complication during this procedure is the presence of leaks in the anastomosis line, and this complication was carefully addressed through a seal by a single suture for six of the women in the Swedish trials.[24] In addition, due to the essential nature of proper blood flow, the complication of bleeding during surgery can be detrimental to the success of the procedure. As a result, blood flow is frequently checked during uterine transplantations to make sure it is at an adequate level. In the case of the Swedish trials, a vascular Doppler probe was used to frequently check for proper blood flow in the recipient during both perioperative and postoperative times.[25]

Along with the necessity for proper blood flow through the uterus, the potential for infection poses another risk to the recipient. In the Swedish trials, the total failure rate was 2 out of 9 women, with one of the women suffering an artery thrombosis, and the other developing a Enterococcus faecalis infection postoperatively.[25] Likewise, in the Cleveland Clinic's first attempt at a uterine transplantation with a dead donor, a Candida albicans fungal infection developed postoperatively in the recipient.[12] Even though the organ procurement organization LAORA were aware of the infection, they failed to inform researchers at the Cleveland Clinic about the infection.[13] Without being notified of any issues with the uterus, the Cleveland Clinic inserted the uterus into the recipient. As a result of the lack of communication by LAORA to the Cleveland Clinic, the life of the recipient of the donor uterus was threatened. The recipient experienced restricted blood flow to her implanted uterus through the presence of an infected uterine artery, and the uterus had to be removed 12 days after her initial transplantation.[13] Even after the removal of the uterus, the infection continued to cause complications for the recipient. A week after the initial removal of the uterus, the recipient experienced bleeding in an artery in her left leg that was caused by the infection.[13] In response to this outcome, the Cleveland Clinic mandated that all further trials involve the administration of antifungal medications.[13] Through this failure, it is evident that the proper exclusion of unsuitable donor candidates is vital to the outcome of uterine transplantations.[31] In order to prevent future miscommunications, experts have urged U.S. donor registries to create a single and unified national donor registry.[35]

Perhaps the most important impact of uterine transplants on recipients occurs through the exposure to immunosuppressive drugs, which includes several risks and benefits for the recipient. At the beginning of a uterine transplantation, immunosuppressive drugs are administered to recipients to prevent uterine graft rejection.[5] These immunosuppressive drugs are further maintained while the recipient has the transplanted uterus to continue to avoid uterine graft rejection, which is beneficial to the recipient. Although, in recipients of traditional organ transplantations, one potential risk is that long-term rejection is fairly common, even with administration of immunosuppressive drugs. In the long-term, nearly 50 % of transplanted organs experience rejection after 10 to 12 years.[36] However, since uterine transplants are a temporary procedure, long-term rejection of the uterus is not a major concern. According to Dr. Kathleen O'Neill, the lead researcher in the Penn UNTIL trials, the recipient of the transplanted uterus is typically given around six months to heal before being implanted with embryos through IVF.[37] Dr. O'Neill described how the women that receive a uterine transplantation typically have the uterus for a total of two to three years, which allows the recipients to have up to two births.[37] Through having the uterus for such a short period of time, women that undergo uterine transplantations will not have to fear long-term rejection as in traditional organ transplantations.[37]

Although uterus transplants do not pose long-term rejection concerns, short-term periods of rejection are a concern in all organ transplantations, including uterus transplants. According to Stanford Medicine, an episode of acute rejection within the first year of transplantation occurs in about 25 % of kidney recipients and about 40 % of heart recipients.[38] Due to the prevalence of acute complications, proper administration of immunosuppressive drugs is essential to prevent organ rejection. For all of the reported uterine transplantations in humans to date, combinations of immunosuppressive drugs were used to thwart the rejection of the uterus. In the first uterine transplantation in Saudi Arabia, the recipient was initially given induction therapy via oral corticosteroids preoperatively, along with an oral and IV administration of corticosteroids preoperatively.[31] A combination of oral cyclosporine A, azathioprine, and prednisolone was administered to the recipient to maintain immunosuppression after the surgery.[6] Despite the immunosuppressive medication, nine days after the surgery the recipient displayed signs of acute rejection. The recipient had a subclinical fever, tachycardia, and vaginal discharge, which are signs of acute rejection.[31] The recipient received a temporary increase in her immunosuppressive medications

and the addition of IV corticosteroids; however, the rejection did not subside until the addition of anti-thymocyte globulin, an antibody that protects transplanted organs against an attack from human T cells.[31] Even though the uterus was eventually removed three months later due to a separate undisclosed complication, no further rejection was observed indicating the importance of a proper combination of immunosuppressive medications.

Along with the case in Saudi Arabia, members of the Swedish trials experienced cases of rejection. In the Swedish trials, recipients were also initially treated with induction therapy. The recipients were given mycophenolate mofetil (MMF) preoperatively, and they were all given methylprednisolone perioperatively.[25] In addition, during the surgery, the recipients also received anti-thymocyte antibodies in the form of anti-thymocyte globulin or thymoglobulin, as these antibodies are able to deplete T lymphocytes.[25] After the surgery, maintenance immunosuppressive therapy involved the regular administration of tacrolimus and MMF, with oral glucocorticosteroids given during the first 4 postoperative days. The Swedish trials used a less demanding immunosuppression treatment than previous trials, but the results were extremely promising. Only four of the seven recipients with viable uteri experienced an episode of mild rejection, and these rejections were easily treated by the administration of corticosteroids for 7-10 days, indicating that immunosuppression was close to optimal.[25] The birth of the first baby through a uterine transplantation during the Swedish trial indicated that rejections can be properly managed in patients that experience rejection.

Despite the ability to have an optimal combination of immunosuppressive drugs, these medications pose various short-term and long-term risks. For example, corticosteroids are a common immunosuppressant medication with short-term side effects of high blood pressure, weight gain, glaucoma, and mood swings.[39] Even though these symptoms can be managed, long-term side effects pose greater risks. For example, corticosteroids can lead to the development of osteoporosis and suppressed adrenal gland hormone production.[39] Along with corticosteroids, tacrolimus and cyclosporine have potentially harmful impacts on recipients. Both tacrolimus and cyclosporine have been associated with a decrease in muscle fiber coordination, and a delay in muscle contraction.[40] In addition, azathioprine can potentially result in several side effects, such as nausea and vomiting with occasional stomach pain and diarrhea.[41] One advantage of using azathioprine is that it tends to have less side effects than other immunosuppressant medication; however, it normally takes 6-12 weeks for the drug to become effective in the body.[40]

Even though these immunosuppressant drugs are vital to the success of the organ transplantation, some studies have indicated that they can potentially lead to the development of cancer. In a study of 489 cadaveric renal transplant patients that were randomly assigned to three different immunosuppressive regimes, a total of 226 (46 %) patients developed at least one type of cancer during a median follow-up of 20.6 years.[42] Of the 226 patients who developed cancer, 171 (35 %) of the patients developed at least one type of skin cancer excluding melanoma, while 95 (19 %) patients had at least one type of non-skin related cancer, and there was no significant difference in cancer incidence between the type of immunosuppressive regime administered.[42] In addition, in a National Cancer Institute study of data from over 175,000 organ transplantation recipients, researchers discovered a two-fold risk of cancer for all of the recipients of organ transplants.[43] Evidently, immunosuppressive drugs have the potential to lower the immune system's ability to detect and destroy cancer cells, and can hamper its ability to fight off cancer causing infections.[44] The potential short-term and long-term side effects of these immunosuppressive medications must be described to recipients of uterine transplantations before being administered to ensure the right to informed consent.

In-vitro Fertilization

After the uterus is successfully transplanted, recipients are typically given six months to heal, and then allowed to become impregnated through in-vitro fertilization (IVF): the main type of assisted reproductive technology (ART). According to the CDC, in 2018, 306,197 ART cycles were performed in the United States, resulting in 81,478 live born infants and 73,831 deliveries of at least one infant.45 Of the 306,197 ART cycles, 103,078 were egg or embryo banking cycles, which involves the freezing of eggs and embryos for later use.[45] As the popularity and awareness of IVF has increased, the percentage of infants born from IVF in the United States has steadily increased. Out of the approximately 4 million live born infants in the United States in 2018, nearly 1.9 % of the births resulted from IVF.[45]

Unlike traditional fertilization, IVF involves the fertilization of extracted eggs and sperm in the

laboratory, and the resulting embryo is inserted into the uterus through the cervix.[45] Although the first successful case of IVF resulting in a birth had been done with a single oocyte obtained during spontaneous ovulation, this method was overall unsuccessful for most subsequent cases.[46] In response, investigators implemented ovarian stimulation methods where a woman's ovulatory process is first monitored and stimulated through the administration of synthetic exogenous hormones, such as follicle stimulating hormone (FSH) and luteinizing hormone (LH).[47] Another method used to stimulate ovulation includes use of selective estrogen receptor modulators (SERMs), including clomiphene and tamoxifen. However, it has been observed that the use of exogenous FSH yields a higher oocyte count than with the use of SERMs.[46] For controlled ovarian stimulation, there are long and short protocols that are used. During the long protocols, medications, which include either Gonadotropin-releasing hormone agonist or antagonist or oral contraceptive pills, are administered during the menstrual cycle before the IVF cycle.46 The short protocols involves starting medications during onset of the natural menstrual cycle, where human menopausal gonadotropins (hMG) or FSH is administered to achieve controlled ovarian stimulation and either a GnRH agonist or antagonist is used to block spontaneous ovulation. 34 to 36 hours after administration of human chorionic gonadotropin (hCG), oocytes are retrieved via the transvaginal ultrasound guided follicle aspiration method, with the use of analgesia or anesthesia.[46] With direct ultrasonographic visual guidance, a needle is inserted into each follicle and the contents are subsequently aspirated. These recovered oocytes are then mixed with spermatozoa and are allowed to incubate in a small volume of culture medium to achieve fertilization.[46] For women that underwent a uterine transplantation, a major benefit is that embryos can be directly inserted into their uterus instead of the traditional use of a gestational carrier for women with UFI. A simple blood test approximately two weeks after embryo injection can confirm if pregnancy has been successfully achieved.[47]

Despite the benefit of IVF allowing women that undergo uterine transplants to birth their own children, there are several risks to the procedure. For example, the most profound risk of IVF is the presence of multiple births. According to the CDC, in 2016, infants born from IVF are more likely to be multiples (31.5 %) versus singletons (68.5 %) when compared to the rates of 3.4 % multiples and 96.6 % singleton for the general population of infants born in the United States.[48] Multiple birth pregnancies can be detrimental to mothers as they have an increased chance of complications like miscarriage, high blood pressure, premature labor, placental abnormalities, and pre-eclampsia.[49] Along with multiple births, the injectable hormones that are utilized in IVF can result in the development of a rare condition known as ovarian hyperstimulation syndrome (OHSS). OHSS typically presents with the presence of swollen and painful ovaries, and includes symptoms of mild abdominal pain, bloating, nausea, diarrhea and vomiting that last about a week.[47] In more severe cases of OHSS women can experience shortness of breath, rapid weight gain, and faintness.[50] Fortunately, OHSS is a rare complication that many women utilizing IVF will not have to worry about experiencing. According to the Cleveland Clinic, OHSS occurs in less than 5 % of women who receive IVF, with severe cases of OHSS happening in less than 1 % of women.[51]

Similar to the chance of developing OHSS, women who undergo IVF have a slight chance of an ectopic pregnancy: a pregnancy where the fertilized egg implants outside of the uterus, typically in the fallopian tube. According to the Mayo Clinic, approximately 2 to 5 % of women that utilize IVF will endure an ectopic pregnancy, resulting in the pregnancy not being able to go to term.[47] With such a small chance of enduring an ectopic pregnancy, this complication is not a major concern to women using IVF. Furthermore, the egg removal process of IVF carries some inherent risks. For example, during egg retrieval, women can be subjected to bleeding, infection, and damage to the bowel or bladder. Women who use IVF also face psychological and emotional risks. While utilizing IVF, women can be burdened with psychological stress and the feeling of being emotionally drained, especially if IVF is unsuccessful.[50]

Even though IVF is a relatively straightforward procedure, the success of IVF depends on numerous factors. For example, one major determinant of the success of IVF is the age of the recipient. For women younger than 35, the likelihood of having a full term, normal birth weight, and singleton live birth per IVF cycle is greater than 20 %.[52] However, the likelihood of women older than 35 of achieving these conditions per IVF cycle is drastically reduced. For example, women 35 to 37 years old have a 17 % chance, women 38 to 40 years old have a 11.1 % chance, women 41 to 42 have a 5.7 % chance, while women older than 44 have a 0.6 % of achieving a live birth per IVF cycle.[53] To increase the chances of a live birth, women over the age of 41 are advised to use a younger donors eggs rather

than their own eggs.[47] Along with age, lifestyle factors can influence the success of IVF. According to the Mayo Clinic, smoking can lower a woman's chances of IVF by 50 %.[47] Furthermore, the embryo status and reproductive history can affect the success of IVF. For example, more developed embryos tend to lead to higher pregnancy rates, and success rates for woman who did not get pregnant from previous rounds of IVF are lower.[47] The cause of infertility can also play a role in the success of IVF. According to the Mayo Clinic, women with conditions like severe endometriosis are less likely to get pregnant than other types of infertility.[47] Evidently, the ability of IVF to develop a successful pregnancy depends on several critical factors that vary between women.

Impact on Offspring

The impact of uterine transplantation on the developing offspring is another important component of uterine transplantations. For organ transplantation recipients that are pregnant, there is a general increase in the presence of obstetric complications, such as preeclampsia, miscarriage, premature delivery, low birth weight.[31] In terms of uterine transplantations, the most common complications include preterm delivery and low birth rate. According to Penn Medicine, all babies who have been born by uterine transplants to date have been born premature, mostly between 35-37 weeks via cesarean section.[2] These babies are stated to be purposely born early to ensure the health of the mother and the child.[2] A premature birth can potentially be problematic, as premature babies typically have a low birth weight, which can lead to a higher chance of complications. According to the Children's Hospital of Philadelphia (CHOP), premature babies with a low birth weight are at risk for having trouble breathing, eating, preventing infection, and gaining weight.[54] Due to these potential complications from a low birth weight, many premature babies struggle to survive. The World Health Organization reports that approximately 60 % to 80 % of all neonatal deaths are influenced by the presence of a low birth weight.[55] Despite being born premature with a low birth weight, all of the babies that have been born through uterine transplants have been cited to have no other complications. However, premature babies still have the potential to develop long-term visual and hearing problems, and learning disabilities.[56]

Along with the potential harmful effects of premature birth, the immunosuppressant drugs could potentially cause abnormalities during birth. All immunosuppressant drugs have the ability to cross the placenta, which could impact the development of the fetus. Even though development during the first trimester is unlikely to be affected, the administration of immunosuppressive medications during the second and third trimester increases the risk of a low birth weight, and can lead to a transiently compromised immune system for the fetus.[57] Despite these risks, there have been no reports of babies born through uterine transplantations having genetic defects. With the proper administration of medicine and routine follow up visits, Penn Medicine has reported that there has been no increase in congenital abnormalities in babies born via uterine transplantation.[19] However, Dr. O'Neill stresses that more research must be done to understand the potential long-term influence of immunosuppressant medications on offspring conceived through a transplanted uterus.[37]

Without the presence of congenital abnormalities in babies born via uterine transplantation to date, couples have not had any reason to terminate their pregnancy early. However, ethical issues like abortion may arise in the future if a fetus is detected to have a genetic abnormality before birth. A genetic abnormality may compel the couple to terminate the pregnancy early. In the United States, approximately 18% of pregnant women in 2017 had an abortion.[58] Since abortion is an option for fertile women, will infertile women who undergo uterine transplantations still have the ability to have an abortion? While the feasibility of abortion in women who have received a uterine transplantation is unknown, this could potentially pose a threat to the fetus. This ethical issue must be further examined in the future when more research is available on the subject.

FINANCIAL COSTS:

Similar to many other organ transplantation procedures, the cost of a uterine transportation is expensive. According to a Milliman Research Report in January 2020, the total billed charges for a single kidney transplant is approximately $450,000, while the total billed charges for a heart transplantation is approximately $1,700,000.59 With private insurance, Medicare, and Medicaid, the out-of-pocket cost for the recipient is typically much lower. However, many recipients of organ transplants still struggle to pay for their procedures. Medicare and private insurance usually does not cover 100 % of an organ transplantation, which leaves deductibles and other expenses for the recipient.[60] Since private insurance varies based on location and coverage, costs for the recipient are variable. In addition, only certain types of organ transplantations are covered by Medicare and

private insurance, which further burdens recipients with out-of-pocket costs.[60] Evidently, quality insurance does not guarantee an affordable out-of-pocket cost. As a result, GoFundMe campaigns have become a vital way for individuals to raise money for their procedures with around 33 % of all campaigns on the platform citing medical needs.[61] Since uterine transplantations are considered to be a nonessential surgery, insurance coverage does not apply to the procedure.

Without insurance coverage, recipients of uterine transplantations are burdened with high out-of-pocket costs. Despite still being in clinical trials, Baylor Medical Center estimates that uterine transplantations cost around $200,000.[62] Due to these expensive costs, researchers are taking on the out-of-pocket costs to encourage women to participate in their trials. For example, Penn Medicine covered the entire cost of JG's transplant, which was estimated at half a million dollars.[63] Evidently, there are other outside costs besides the cost of the transplantation procedure. One of the major outside costs of the procedure involves the required administration of immunosuppressive medications. Without immunosuppressive medications, the transplanted organ is likely to be attacked by the recipient's immune system. In the United States, immunosuppressive medications cost upwards of $2,500 a month, and the average cost per year of these medications ranges between $10,000 to $14,000.[64] With these high costs, getting insurance companies to cover these medications has proved to be problematic. Recipients of organ transplantations without Medicare have to obtain their immunosuppressive medications through Medicare's drug program, Part D, which is managed by private insurers.[65] One major problem of this system is that private insurers are refusing to pay for many immunosuppressive medications, as some are not FDA approved.[65] As a result, many recipients are forced to ration their immunosuppressive medications, which raises the risk of the rejection of the organ.

Since immunosuppressive medications for uterine transplantations are required throughout a recipient's pregnancy, costs for these immunosuppressive drugs can become astronomical. Recipients of uterine transplantations typically discontinue their immunosuppressive medications after the birth of up to two healthy babies.[19] In addition, recipients of uterine transplantations need time to recover after their surgery. This required healing period resulted in an embryo being introduced into JG nearly 6 months after surgery. Due to the extended period of time with the uterus, recipients will potentially have to pay for immunosuppressive medications for many years, which can become extremely costly overtime.

Along with immunosuppressive medications, IVF is another expensive component for women that seek to utilize uterine transplantations. A single cycle of IVF costs approximately $12,000 to $17,000 without medication, and can rise to nearly $25,000 with the use of medications that induce ovulation.[66] However, the national average success using IVF takes between 2 and 3 cycles, with one cohort study identifying the average to be around 2.7 cycles.[67] Evidently, several rounds of IVF is extremely expensive for patients, especially if cycles of IVF are unsuccessful. In addition, the costs of IVF can be increased by thousands of dollars with optional additions to the procedure, such as genetic testing of embryos and additional surgical procedures like sperm extraction and laparotomy.[66] Furthermore, similar to immunosuppressive medications, the insurance coverage of IVF is complex. As of August 2020, 19 states have passed legislation including fertility insurance coverage laws, with 13 of those states including IVF coverage.[68] Even though some insurance policies include coverage for both IVF and the necessary medications, Penn Medicine notes that not all insurance plans cover fertility care, resulting in out-of-pocket fertility care costs for patients.[53]

After IVF is performed, the need of a hysterectomy to remove the uterus after having children also increases the total cost of the procedure. It is estimated that a typical elective hysterectomy costs around $32,000 for vaginal, $38,000 for laparoscopic, $44,000 for abdominal, and $50,000 for robotic hysterectomies.[69] Insurance coverage typically varies for elective hysterectomies with some insurance companies covering nothing for the recipient. Clearly, efforts must be made to lower the cost of uterine transplantations to make them affordable and accessible for more women. Access to the procedure would greatly benefit minority groups, as studies have shown that African American women in particular are two-fold more likely to experience infertility in comparison to Caucasian women, even after adjusting for socioeconomic status, risk factors, and pregnancy intent.[70] However, Dr. O'Neill from Penn Medicine expressed her uncertainty with the total cost of the procedure, but emphasized that uterine transplantations will certainty cost over $100,000.[37] As a result, this may limit access to uterine transplantations to women from high socioeconomic statuses, unless insurance coverage is able to extend to this non-life-threatening procedure.

ETHICAL ANALYSIS:

The issue of uterine transplantation has raised serious interdisciplinary concerns. Many ethicists have called for a public debate on the issue of uterine transplantation that would examine all aspects of it including the ethical and moral implications. These issues include whether uterine transplants should be from live donors or deceased donors. The advantages of using deceased donors, as stipulated above, include eliminating surgical risks to live donors, and the ability to harvest more blood vessels from the organs as compared to a live donor organ. Proponents argue that dead-donor transplantation can increase the supply of organs, but there is always the concern that organ donors may not fully understand this type of non-life-threatening organ donation. Other issues that arise are the complications to the recipient of this nonessential and temporary procedure, the potential side-effects of the immunosuppressants for the mother and the fetus and finally the cost factors. If this is going to be an open debate with all parties participating, then all options must be placed on the table, including the option that we should not proceed with uterine transplantations. To determine if this procedure is ethical, the principles of respect for persons, beneficence, nonmaleficence and justice will be applied to this procedure and its consequences.

Respect for persons

This principle incorporates two ethical convictions: first, that persons should be treated as autonomous agents; and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.[71] Respect for human persons refers to the right of a person to exercise self-determination and to be treated with dignity and respect. All people deserve autonomy and to be treated with dignity and respect. Failure to provide any person with adequate health care, which includes clinical research and trials, violates this basic right of respect for persons. Appropriate funding for clinical research will increase our understanding of UFI, which will inform future research, and hopefully should result in the development of new, more effective therapies. These therapies could provide the potential to be a third viable option for women with UFI that allows them to carry and deliver their own biological babies.

Second, as an autonomous agent an individual has the right of informed consent. Patients/research subjects have the right to know all information about their diagnosis, prognosis, treatment and care plan. The elements of informed consent include:

1. A fair explanation of the procedures to be followed, including an identification of those which are experimental;
2. A description of the attendant discomforts and risks;
3. A description of the benefits to be expected;
4. A disclosure of appropriate alternative procedures that would be advantageous for the subjects;
5. A offer to answer any inquiries concerning the procedures;
6. An instruction that the subject is free to discontinue participation in the project or activity at any time.[72]

In a specific sense, the surgeons who want to perform the uterine transplants have an ethical obligation to give an objective, non-biased assessment of all materially relevant information pertaining to the success of uterine transplants, risks/benefits, alternatives and consequences. In addition, the rates of rejection, the costs of surgery and immunosuppressant drugs, potential side-effects of the immunosuppressant drugs on the patient and fetus and the psycho-social issues, must be carefully stated and explained to the patient. The surgeons are also responsible to verify, to the best of their ability, that the patient can comprehend and has comprehended the information and has not engaged in "selective hearing." Under the circumstances, it is not uncommon for patients to engage in "selective hearing," that is, taking in all information about potential benefits and filtering out all information about potential risks. In addition to this, surgeons must be vigilant against their influence over subjects, who may unwarily treat the surgeon with the same deference as they treat their primary care physicians. Dr. Robert Levine, professor of Medicine at Yale University, describes the surgeon/researcher's obligation as one of "forthright disclosure." This includes preliminary evidence and data from animal studies and previous human clinical trials that indicate the risks and benefits as well as the safety and efficacy of these controlled studies.[73] Patients need to have information that a prudent person would require to make well-reasoned decisions that will protect their personal interest.

The problem is determining what sort of knowledge translates to what degree of risk to patients. This is a value judgment that must be made by the surgeons. The concern is that the judgment of some surgeons may be biased by considerations of career self-interest and even financial gains.[74] "The potential for coercion can be difficult for

surgeons. On the one hand, most accept that the final choice for surgery should be left to the patient. On the other hand, surgeons want what they believe to be best for their patients. Therefore, there is ample room for unintentional coercion through selecting information for disclosure that overtly reinforces the surgeon's beliefs."[75] There is also the problem of forming an "innovative alliance." Patients may encourage their surgeons to try any new and promising technique to improve their quality of life or prospects for survival and surgeons also may be eager to apply a promising new technique for the same reasons. It is the duty of the surgeons to decide whether responsible behavior lies in attempting an innovative technique or in concluding that the background research is not sufficient to warrant its use, even when the patient consents.[76] The surgeon has the responsibility to act in the best interest of the patient. The belief that this experimental surgical procedure will not cause too much harm to too many people or that society will benefit at the possible expense of particular individuals violates the duty of the surgeon/researcher to act in the best interest of the patient. To determine whether that duty has been breached, a surgeon/researcher's actions should be measured against the accepted practice as set by professional norms. Those researchers whose treatments fall below the professional standards and cause harm to patients may be held civilly liable for that failure.[77] Various ways have been proposed that ensure individuals going into research protocols are giving informed consent, these include: written and oral forms of consent so that the patient has time to read and reflect on the risks and benefits; someone other than a member of the surgical team obtains the informed consent; obtaining second opinions from other knowledgeable physicians regarding the feasibility of such a procedure; and appointing an objective advocate who would accompany the patient during the decision-making process. These advocates would ensure that the patient is capable of understanding the information and comprehends all the information, that researchers do not overestimate potential benefits and underestimate potential risks, and that all viable options are given, even the option of no transplant. These are not only excellent safeguards; they should be implemented with every research protocol.

Medical advances are necessary for society, and experimental surgeries are important tools to bring about these advances. But these advances can never be at the expense of denying individuals their basic dignity and respect. If patients are made aware and comprehend the success data, short-term and long-term risks and benefits, alternatives and possible consequences and safeguards are put in place to avoid the potential for coercion, then informed consent can be obtained ethically for this procedure.

Beneficence/Nonmaleficence

Beneficence involves the obligation to prevent and remove harm and to promote the good of the person by minimizing the possible harms or risks and maximizing the potential benefits. Beneficence includes nonmaleficence, which prohibits the infliction of harm, injury, or death upon others. In medical ethics this principle has been closely associated with the maxim Primum non nocere: "Above all do no harm."

Proponents of uterine transplants argue that this surgery is a viable option for women to escape the emotional burdens associated with infertility. This procedure is the only biological option for women with UFI to become pregnant and to experience the emotions of carrying a child in their womb. The research is quite clear that using deceased donors is safer than living donors. There is no donor risk, surgical dissection time is shorter, larger diameter blood vessels can be used to simplify the uterine transplantation procedure and there is the opportunity to increase the supply of uteruses for women. Opponents to uterine transplants in general argue this is a non-life-saving procedure that places these women at great risk. The surgical transplantation surgery can take up to 10 hours exposing the patient to serious side effects of lengthy exposure to general anesthesia. There are possible surgical complications such as the presence of leaks in the anastomosis line, complications of bleeding during surgery, the potential for infection such as Enterococcus faecalis experienced by a recipient at the Cleveland Clinic and the potential effects of immunosuppressive drugs on the patient and the fetus. As stated above, there are complications but if deceased donors are utilized and surgeons use robotic-assisted uterine transplantation to decrease the time of the recipient's surgery, some of the potential surgical complications can be minimized. To address the possibility of potential infections, donors will need to be screened more carefully and all further trials will involve the administration of antifungal medications. The immunosuppressive drugs do present potential risks, but the transplanted uterus is temporary. The amount of time the patients will be on these drugs will be far less than if the patient had a kidney, lung or heart transplant. To date, no children born from a uterine transplant have experienced any genetic defects due to the

immunosuppressive drugs. In regards to obstetric complications, the most common complications include preterm delivery and low-birth rate. In the majority of deliveries to date, most women experienced premature births mostly between 35-37 weeks via a caesarian section. These medical complications are not insurmountable. Children have been born safely and free of any genetic anomalies or physical complications.

Many opponents to uterine transplantation will argue that the unnecessary medical complications that could lead to death, outweigh any benefit to these patients. This is a non-essential and temporary procedure that places both mother and child at unnecessary risks. In addition, there is a viable option for these women, which is adoption. This option would not only benefit the children in need of adoption, but those women who desire to be parents and society as a whole. However, after reviewing the facts concerning the state of our knowledge regarding the rate of rejection, possible medical complications, the effects of immunosuppressant drugs on mother and child, and the inevitable psychological impact on the recipient, it is clear that this surgery does everything possible to minimize the risks incurred by these patients. Yes, this surgery does expose them to unnecessary risks that have the potential for injury and harm; however, their desire to be a biological parent would outweigh these risks and complications. This is an experimental, non-lifesaving surgery with serious risks, but it is also a surgery with substantial benefits. Arguably, it appears that this surgery does not fail the test of beneficence or the test of nonmaleficence. No one will dispute that balancing the benefits and risks is difficult. Some will continue to argue that the risks outweigh the benefits. However, if these women truly have informed consent and understand the risk/benefits, alternatives and consequences of uterine transplants, then they have the right to agree to this experimental procedure. For many women, their desire to be a biological mother clearly outweighs the possible medical risks to them.

Justice

The principle of justice recognizes that each person should be treated fairly and equitably, and be given his or her due. The issue of experimental uterine transplants also focuses on distributive justice: the fair, equitable, and appropriate distribution of medical resources in society. At a time when reforming healthcare in this country has become a high priority, failure to initiate preventative measures and clinical research that would save medical resources and possibly human lives in the long-run violates the principle of distributive justice.

The principle of justice can be applied to this situation in two ways. First, questions of justice have been raised about whether those patients who have UFI might be classified as vulnerable individuals and whether this type of experimental surgery is a form of exploitation. No one seems to dispute that surgeons have the skills and techniques needed to perform this transplant surgery. However, opponents argue that there seems to be a competition present among the surgical teams worldwide. This debate cannot and must not be framed within the aspirations of the surgeons. There must be equality between the surgeons and the possible recipients. To allow these charismatic surgeons to present this form of transplantation in the media in such a way that seems to trivialize the side-effects and downplay the possibility of rejection and even death, is to exploit these recipients and use them as a means to an end. At the present time the debate among the transplant surgeons is on how they should proceed. Advancing this experimental surgery can lead to a viable option for woman with UFI. Failure to make surgical advances delays the necessary knowledge these surgical teams need to perfect and advance this procedure. Opponents argue that with this attitude, how objective and unbiased will the information about the surgery and its possible benefits and risks be that will be disclosed to potential recipients? Are these potential recipients not in some cases desperate to be biological mothers? How will surgeons know when the potential vulnerability of some patients is unduly influencing their willingness to consent? Proponents argue these transplant surgeons have suggested ways they believe will ensure informed consent. Yes, this is a non-life-saving transplant and there are other viable options, however; one could say it is unjust to deny women who have UFI a viable option that has been successful and would allow them to carry and deliver their own babies.

Second, the issue of justice pertains to uterine transplantation specifically in regards to distributive justice, which concerns the fair and equitable allocation of medical resources. The main issue here is research priorities. Should funds be used to support uterine transplantation surgery now when the risks seem unreasonable and even deadly? The amount of money spent on these surgeries, which is estimated at $200,000 for the surgery, $20,000 for IVF and $10,000-$14,000 per year for immunosuppressive drugs, could certainly be invested in new ways to resolve infertility problems that impact thousands of women worldwide. This

could potentially benefit many women especially those who are without insurance and could not afford these expensive surgeries. Also, immunosuppressant drugs cost tens of thousands of dollars a year. Will this not limit the individuals who would qualify for this surgery? If so, this now becomes a social justice issue, because those who would have access to this technique would logically be those who are privileged. The poor, the uninsured, the underinsured, and many middle-class individuals would never be viable candidates for this surgery, because they could not afford the cost of the immunosuppressant drugs. In addition, presently, this surgery is not available to transgender women. Is this not a form or injustice? As a matter of social justice, who this surgery would benefit and whether it is a fair and equitable allocation of medical resources is an important ethical issue. Medical professionals have an ethical obligation to use available resources fairly and to distribute them equitably. However, critics have used and continue to use these arguments for all experimental procedures. These are the same arguments that were used when organ transplants were proposed. Unless research is advanced, medicine will never meet the needs of individuals and society as a whole. Yes, at the beginning these procedures will be expensive, but as the procedures are perfected, and new research is advanced, it is inevitable that more and more people will benefit from these clinical trials. The issue of transgender women not being accepted into these clinical trials is a justice issue, but the argument is that until the procedure is perfected, it would not be beneficial to include these women at the present time. Yes, transgender women are excluded now from this experimental procedure, but once this procedure is determined to be safe and effective, these individuals may benefit the most from uterine transplants. As a matter of social justice, who this surgery would benefit and whether it is a fair and equitable allocation of medical resources is an important ethical issue. Medical professionals have an ethical obligation to use available resources fairly and distribute them equitably. As a matter of justice, medical professionals believe that uterine transplants are safe and effective and have the potential to help women with UFI and other conditions to have their own biological children. One can argue that this is a fair and equitable use of medical resources and thus meets the test of the principle of justice. At the present time, if uterine transplantation is being shown to be an effective way of treating women with UFI and the risk-benefit ratio is reasonable, and safeguards are put in place to assure patients have informed consent, then physicians have an ethical obligation to perfect the safety and efficacy of this technique.

RECOMMENDATIONS FOR SELECTION OF DONOR AND RECIPIENTS:

To maximize the success of uterine transplantations for women with UFI, a combination of the selection criteria for donors and recipients from Penn Medicine, Cleveland Clinic, and Baylor University Medical Center should be utilized.[2,78,79] The recommended criteria for eligible recipients for uterine transplantations include:

1. A women of child-bearing age (21-39 years old);
2. Uterine factor infertility;
3. Cancer-free for at least five years;
4. Negative for blood-borne illnesses including HIV, Hepatitis B, and Hepatitis C;
5. No previous history of diabetes or hypertension;
6. Lives within 100 mile radius of medical facility performing uterine transplantations;
7. Must pass an in-depth health screening by experts, including passing a psychological evaluation to affirm competency;
8. Informed consent from the recipient.[2,78,79]

While uteruses for uterine transplantations can be obtained from either live or dead donors, dead donors eliminate the possibility of surgical complications to live donors, and are therefore preferred. The recommended criteria for obtaining a uterus from a dead donor is as follows:

1. A deceased women 18-40 years old;
2. Informed consent from the next of kin;
3. Adequate screening by organ procurement agencies for any microbial infections or diseases that would limit the viability of the uterus.[2,78]

Although dead donor uteruses are preferred, live donor uteruses could also be utilized to increase access to uterine transplantations for women with UFI. The recommended criteria for selecting an eligible live donor for uterine transplantations include:

1. A woman aged 30-50 years old that has completed her own childbearing process;
2. No history of uterine factor infertility;
3. Cancer-free for at least five years;
4. Negative for blood-borne illnesses including HIV, Hepatitis B, and Hepatitis C;
5. No previous history of diabetes or hypertension;
6. Must pass an in-depth health screening by experts, including passing a psychological evaluation to affirm competency;
7. Informed consent from the donor.[79]

Even though these recommendations are based on the current status of uterine transplantations, they are subject to change when more research becomes available on the topic. Especially for transgender women who could potentially

benefit the most from this procedure, the selection criteria can be expanded to include transgender women when the procedure is mastered and deemed safe for these individuals. In addition, while these criteria specifically refer to the pre-uterus transplantation process, monthly health checkups with physicians should be utilized throughout the entire uterine transplantation process to ensure the safety and efficacy of the procedure. At any time in the process, the recipient of uterine transplantations should have the right to discontinue the treatment.

CONCLUSION:

Uterine transplantations are an extremely promising procedure for women with UFI that allows them to carry and deliver their own babies. While the procedure is still in experimental trials, it has tremendous potential to change the lives of thousands of women throughout the world with UFI. Despite the potential risks to the recipients, donors, and offspring of the procedure, the risk-benefit ratio is reasonable, and therefore this treatment should be mastered assuming proper safeguards are put in place. When this procedure is perfected, then it can hopefully be expanded to the transgender community, who would greatly benefit from access to uterine transplantations. While uterine transplantations are a couple years away from public access, one facet is explicitly clear: They provide a potentially safe and effective alternative to the traditional options of surrogacy and adoption for women suffering with UFI.

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