Uterus transplantation
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The last frontier to conquer in female infertility is absolute uterine factor infertility (AUFI), affecting around 200,000 women in Europe. Causes of AUFI are multiple such as absence of a uterus from birth (MRKH-syndrome) or through hysterectomy (cervical cancer, myoma, peripartum emergency hysterectomy). In other women with AUFI the uterus can be present but non-functional in terms of being able to carry a pregnancy (Ashermans´s syndrome, myoma, uterine malformation).

Uterine transplantation (UTx) is now the first available treatment for this large group of women. Adoption and gestational surrogacy are other means to obtain motherhood, but the acceptances of these arrangements in the society vary greatly between societies.

Our research group initiated a step-by-step developmental animal-based research approach on UTx in 1999 and have optimized all aspects of the procedure in several animal species. Today 11 human UTx attempts have been made, with the last 9 of them performed by our team. The first two human UTx-attempts were done in Saudi Arabia in 2000 and in Turkey in 2011. Both these teams had no research experiences in the field. These two transplantations have not been successful.

In early 2013 our team completed the surgeries of a series of totally 9 human UTx, with live uterus donors. Eight recipients were MRKH patients and one had been hysterectomized because of cervical cancer 7 years prior to transplantation.

The mean age of the recipients was 31.5+/-3.9 years. Five donors were mothers and this included the donor of the cervical cancer patient. Other donors were close relatives and in one case family friend. The mean age of the donors was 53.0+/-7.0 years. IVF treatments were done before transplantation. The donor surgery involved uterine isolation with pedicles of the uterine arteries and veins and including large parts of the internal iliacs. The duration of these surgeries were between 10h 17min and 13h 8min (11h 37 min +1h 54 min). No donor needed perioperative blood transfusion and the hospital stay was 6 days. One complication occurred, with a uretero-vaginal fistula in donor #2 two weeks after surgery and repaired 3 months later.

In the recipient a midline incision was used and the external iliac artery and vein were mobilized bilaterally. Bilateral end-to-side anastomosis was accomplished between the uterine artery and one major uterine vein on each side, using 7-0 and 8-0 sutures on arteries and veins, respectively. After commencement of uterine perfusion the vaginal-vaginal anastomosis was accomplished. The graft was fixed to the round, cardinal and sacrouterine ligaments and an extensive leaf of bladder peritoneum of the graft was sutured on top of the bladder for extra structural support. The duration of recipient surgery operations varied between 4h 10min and 5h 56min (4h 46min + 30min). None needed perioperative blood transfusion and the hospital stay varied between 3 and 9 days. The recipients received two ATG treatments perioperatively and corticosteroids for 4 days. They were then only on double immunosuppression with tacrolimus and MMF and the plan was tapered doses of tacrolimus and omission of MMF after 6 months, to avoid possible teratogenic effects of MMF.

Two patients had to be hysterectomized during the initial months due to uterine complications. In recipient #2, an intrauterine infection (Enterococcus faecalis) was diagnosed 33 days after UTx and despite repeated attempts with iv antibiotics and surgical drainage the infection progressed with septic symptoms necessitating hysterectomy 105 days after UTx. In recipient #9 (Leiden mutation heterozygote) uterine artery thrombosis was diagnosed on the 3rd postoperative day and a non-perfused uterus was removed.

Mild rejection episodes have occurred in 5 of the seven successfully transplanted patients and all have been reversed by 7-10 days of corticosteroid treatment. All these seven patients have shown regular menstruations from 2 months after UTx. Embryo transfers have started in all 7 patients during the spring of 2014. The first livebirth after UTx occurred in September 2014 when a healthy male baby was delivered by c-section in week 31+5 because of maternal preeclampsia (PE) development. Since then two more births have taken place and these mothers did not develop PE. Two miscarriages (week 6 and 14) have occurred and presently uterine recipient is pregnant in her second trimester. Only one of the 7 good (graft survival past 12 months) transplants has so far shown implantation failure (no pregnancy in 4 SET attempts).
The successful pregnancies after UTx are proofs-of-concept of UTx as a relatively effective method to treat uterine factor infertility. More observational studies should follow to optimize the live donor surgery, so that in particular the surgical duration of the donor can be shortened, and to demonstrate that also deceased donor uterus transplantation is successful in terms of birth of a healthy baby.
Ovarian cryopreservation was established in two centres in Sweden (population 9.5 million) already in 1998. In the beginning various cryopreservation protocols were used. The most well-structured program for fertility preservation in Sweden during the last decade has been that of Karolinska University Hospital in Sweden. In this lecture the characteristics of the patients that have undergone ovarian cryopreservation in Sweden will described. A small number of retransplantation attempts have been made and in 2013, the first live birth occurred from a patient of the Karolinska Hospital cohort. This was from a women with Hodgkin’s disease, who had been treated with both chemotherapy and radiation therapy. Her uterine size was decreased.

In conclusion, the lecture will give a summary of the Swedish efforts and clinical success in ovarian cryopreservation.