Anthem

Medical Policy

Subject: Uterine Transplantation
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Description/Scope

This document addresses uterine transplantation, which has been proposed as a treatment of uterine factor infertility. This procedure involves the transplantation of a healthy donor uterus obtained from living or recently deceased donor into an individual with a nonfunctioning or absent uterus. The scope of this document is limited to the transplant procedure only, and does not address other related infertility treatment or obstetric services.

Note: Please see the following for additional information:

- CG-SURG-34 Diagnostic Hysteroscopy for Infertility

Position Statement

Investigational and Not Medically Necessary:

Uterine transplantation is considered **investigational and not medically necessary** for all uses, including but not limited to the treatment of uterine factor infertility due to nonfunctioning or absent uterus.

Rationale

Uterine transplantation has been proposed as an alternative to adoption and surrogacy for individuals with uterine factor infertility (UFI) as a result of nonfunctioning or absent uterus. The process starts with creating an embryo using in vitro fertilization (IVF) in which the women's eggs are harvested, fertilized, and cryopreserved for transfer into the uterus following transplantation. A healthy uterus from a living or recently deceased donor is transplanted into the recipient. After approximately 6-12 months, if the transplanted organ has been deemed viable and functional a single embryo IVF implantation procedure is conducted. If the procedure leads to a successful pregnancy, the pregnancy is treated as high-risk and the child is delivered via Cesarean section at approximately 37 to 39 weeks. After one or two successful deliveries the transplanted uterus is removed via hysterectomy to avoid the continued need for immunosuppressive medication (Brännström, 2014).

Johannesson and colleagues (2015) reported primary outcomes from a prospective case series of human uterine transplantation from live donors (NCT01844362). The study enrolled 9 participants presenting with absolute UFI and viable uteri after undergoing live-donor uterine transplantation. The measured outcomes included menstruation, uterine artery blood flow, histology of cervical biopsy, and blood levels of tacrolimus. After the initial 6-month period, uterine grafts were removed in 2 participants, 1 related to persistent intrauterine infection and the other due to bilateral uterine vessel thrombosis. The authors reported initial 12-month outcomes on the 7 remaining participants, all of whom had normal menstrual patterns and uterine blood flow. A total of 9 rejection episodes (n=5) were reported; all cases were subclinical and asymptomatic, and detected by cervical biopsy. All resolved by temporary therapy with glucocorticoids.

The 2018 American Society of Reproductive Medicine (ASRM) position statement on uterus transplantation offers the following committee opinion:

- Uterus transplantation is an experimental procedure for the treatment of absolute uterus-factor infertility.
- Uterus transplantation should be performed within an IRB-approved research protocol.
- A uterus transplantation program requires a multidisciplinary team experienced with the technique prior to attempting transplantation in human subjects.
- The organ used during uterus transplantation can be from living or deceased donors; each approach has its own challenges and strengths.

  Uterus transplantation is an experimental procedure that may allow women with absolute uterus-factor infertility to achieve a pregnancy.

Johannsson and colleagues (2022) reported initial outcomes data from first study of uterus transplantation from 5 years, collected from three United States centers between 2016 and 2021. This cohort study of 33 uterus transplants that were performed, 21 (64%) transplantations from living donors and 12 (36%) from deceased donors, with a 74% (n=23 of 31 recipients) 1-year graft survival. A total of 58% of participants (19 of 33) transplanted achieved at least 1 live birth, 83% of recipients (19 of 23) with a viable graft at 1 year achieved at least 1 live birth post-transplant. All neonates were born live with median gestational age of 36 weeks and 6 days. The results of the study were conducted in conjunction with a clinical trial and cannot be generalized.

Coleman and colleagues (2022) address uterus transplantation in the standards of care for the health of transgender and gender diverse people (version 8). In summary the authors conclude:

> Statement 10.12
> We suggest health care professionals caring for individuals with intersexuality and congenital infertility introduce them and their families, early and gradually, to the various alternative options of parenthood.
>
> While uterus transplantation has had preliminary success in people with Mullerian agenesis, there is no protocol to date that avoids exposure of the developing fetus to the risk associated with the medication used to avoid transplant rejection.

There are recruiting and ongoing clinical trials studying uterine transplantation for treatment of uterine factor infertility due to congenital or nonfunctional uterus. However, to date, results from these studies have not been published. Data from prospective, long-term studies are needed to determine the safety and clinical utility of the procedure, including potential long-term effects of transplantation and anti-rejection medications on both the mother and the baby. Other proposed uses which may further be explored in the future are the "views of transgender women on their reproductive aspiration, motivations, and desire to undergo uterus transplant should it eventually be proven feasible" (Jones, 2021).

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Background/Overview

According to Centers for Disease Control and Prevention, infertility affects nearly 6% of childbearing-aged women (15 to 49 years) in the United States (CDC, 2022). Nearly 1 per 5000 females is born with müllerian agenesis (also referred to as müllerian aplasia, Mayer-Rokitansky-Küster-Hauser syndrome, or vaginal agenesis), a rare condition caused by embryologic underdevelopment of the müllerian duct, with resultant agenesis or atresia of the vagina, uterus, or both.

The first uterus transplant was performed in Europe in 2014. As of 2021 there have been roughly 80 uterine transplants performed worldwide (Brännstrom, 2021), including 33 in the United States (Johannesson, 2022). Several research studies into this procedure are underway.

Definitions

Institutional review board (IRB): An institutional review board is a group that has been formally designated to approve, monitor and review biomedical and behavioral research involving humans with the aim to protect the rights and welfare of the subjects. The Food and Drug Administration and the Office of Protection from Research Risks (part of the National Institutes of Health) set the guidelines and regulations governing human subject research and IRBs.

Uterine factor infertility: Condition where an individual woman cannot get pregnant because she either does not have a uterus or her uterus is no longer functioning correctly. This can be a result of a congenital condition or an acquired condition.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Investigational and Not Medically Necessary:
For the following procedure codes; or when the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT	
0664T	Donor hysterectomy (including cold preservation); open, from cadaver donor
0665T	Donor hysterectomy (including cold preservation); open, from living donor
0666T	Donor hysterectomy (including cold preservation); laparoscopic or robotic, from living donor
0667T	Recipient uterus allograft transplantation from cadaver or living donor
0668T	Backbench standard preparation of cadaver or living donor uterine allograft prior to transplantation, including dissection and removal of surrounding soft tissues and preparation of uterine vein(s) and uterine artery(ies), as necessary
0669T	Backbench reconstruction of cadaver or living donor uterus allograft prior to transplantation; venous anastomosis, each
0670T	Backbench reconstruction of cadaver or living donor uterus allograft prior to transplantation; arterial anastomosis, each
ICD-10 Procedure	
0UY90Z0	Transplantation of uterus, allogeneic, open approach
0UY90Z1	Transplantation of uterus, syngeneic, open approach
0UY90Z2	Transplantation of uterus, zooplastic, open approach
ICD-10 Diagnosis	
	All diagnoses, including but not limited to the following:
N97.2	Female infertility of uterine origin

References

Peer Reviewed Publications:

1. Brännström M, Belfort MA, Ayoubi JM. Uterus transplantation worldwide: clinical activities and outcomes. Curr Opin Organ Transplant. 2021; 26(6):616-626.
2. Brännström M, Johannesson L, Dahm-Kähler P, et al. First clinical uterus transplantation trial: a six-month report. Fertil Steril. 2014; 101(5):1228-1236.
3. Järvholm S, Enskog A, Hammarling C, et al, Uterus transplantation: joys and frustrations of becoming a 'complete' woman—a qualitative study regarding self-image in the 5-year period after transplantation, Human Reproduction, 2020; 35(8):1855-1863.
4. Johannesson L, Järvholm S. Uterus transplantation: current progress and future prospects. Int J Womens Health. 2016; 8:43-51.
5. Johannesson L, Richards E, Reddy BA, et al. The first 5 years of uterus transplant in the US a report from the United States Uterus Transplant Consortium. JAMA Surg. 2022; 57(9):790-797.
6. Johannesson L, Kvarnström N, Mölne J, et al. Uterus transplantation trial: 1-year outcome. Fertil Steril. 2015; 103(1):199-204.
7. Johannesson L, Richards E, Reddy Vet al. The first 5 years of uterus transplant in the US: A report from the United States Uterus Transplant Consortium. JAMA Surg. 2022; 157(9):790-797.
8. Jones BP, Rajamanoharan A, Vali S, et al. Perceptions and motivations for uterus transplant in transgender women. JAMA Network Open. 2021; 4(1):e2034561.
9. Testa G, Koon EC, Johannesson L, McKenna GJ, et al. Living Donor Uterus Transplantation: A Single Center's Observations and Lessons Learned From Early Setbacks to Technical Success. Am J Transplant. 2017; 17(11):2901-2910.

Government Agency, Medical Society, and Other Authoritative Publications:

1. American Society for Reproductive Medicine. Diagnostic evaluation of the infertile female: a committee opinion. 2015. Available at: Diagnostic evaluation of the infertile female: a committee opinion - Fertility and Sterility (fertstert.org) Accessed

on January 7, 2024.
2. American Society for Reproductive Medicine (ASRM). American Society of Reproductive Medicine position statement on uterus transplantation: a committee opinion. Fertil Steril 2018; 110:605-610.

Websites for Additional Information

1. American Society for Reproductive Medicine. Available at:http://www.asrm.org. January 7, 2024.
2. Centers for Disease Control and Prevention. Infertility FAQs. Last reviewed April 26, 2023. Available at: https://www.cdc.gov/reproductivehealth/infertility/index.htm. Accessed on January 7, 2024.
3. Coleman E, Radix AE, Bouman WP. Et al. Standards of care for the health of transgender and gender diverse people, Version 8. Int J Transgend Health. 2022; 23(1):S1-S259.
4. United Network for Resource Sharing (UNOS). What organs can be transplanted? Available at:https://unos.org/transplant/. Accessed on January 7, 2024.

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Document History

Status	Date	Action
Reviewed	02/15/2024	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Background/Overview, References and Websites sections.
Reviewed	02/16/2023	MPTAC review. Updated Rationale, Background, References and Websites sections.
Reviewed	02/17/2022	MPTAC review. Updated Rationale, Background, References and Websites sections. Updated Coding section to remove NOC code, no longer applicable.
New	02/11/2021	MPTAC review. Initial document development.