# Oocyte cryopreservation and reciprocal in vitro fertilization in a transgender man on long term testosterone gender-affirming hormone therapy: a case report

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**Objective:** To report a successful case of oocyte cryopreservation and subsequent in vitro fertilization (IVF) in a transgender male receiving continued testosterone gender-affirming hormone therapy, followed by reciprocal embryo transfer (ET).
**Design:** A case report of a rare case of fertility preservation in a transgender man with concomitant use of testosterone therapy for 4 years before and during ovarian stimulation.
**Setting:** Private fertility clinic with university affiliation.
**Patient(s):** A 26-year-old transgender man undergoing oocyte cryopreservation before gender-affirming surgery.
**Intervention(s):** Fertility preservation using oocyte cryopreservation and IVF with reciprocal fresh ET into a cisfemale partner.
**Main Outcome Measure(s):** Successful oocyte cryopreservation, oocyte thawing, and reciprocal IVF cycle.
**Result(s):** Oocyte cryopreservation of 29 mature oocytes. Sixteen mature oocytes survived the thaw, and 12 were fertilized with intracytoplasmic sperm injection. A fresh ET of an advanced blastocyst resulted in a clinical pregnancy and live birth.
**Conclusion(s):** Fertility preservation with oocyte cryopreservation or IVF with embryo cryopreservation is feasible for patients on continued long-term testosterone gender-affirming therapy. Future studies on egg quality and reproductive outcomes are required. Our case report demonstrates a promising outcome in this patient population. (Fertil Steril Rep® 2024;5:111–3. ©2023 by American Society for Reproductive Medicine.)
**Key Words:** Oocyte cryopreservation, fertility preservation, ovarian stimulation, testosterone, transgender

The volume of referrals to fertility clinics to offer fertility preservation before initiation of gender-affirming therapy is increasing (1). Although many governing medical bodies advocate for equal and timely access to fertility care for transgender individuals, no clinical practice guidelines exist on how oocyte or embryo cryopreservation should be performed in the transmasculine population (2, 3).

In 2012, Wierckx et al. (4) conducted a survey of 50 transgender men, which concluded that 54% of participants desired family building and over one-third of the surveyed population would have considered oocyte cryopreservation when counseled on option. A retrospective review published by Komorowski et al. (5) in 2021 demonstrated that only 55% of patients were counseled on the impact of fertility on gender-affirming hormone therapy (GAHT). Cessation of GAHT and the gender dysphoria that could result are widely cited barriers in the fertility preservation process (6, 7).

There is scarce literature reporting reproductive outcomes on transgender men who proceeded with ovarian cryopreservation or in vitro fertilization (IVF) although maintaining testosterone therapy. It was commonly accepted to stop testosterone for 3–6 months to allow resumption of menses before starting ovarian stimulation (OS) but this recommendation lacks evidence (8, 9). Furthermore, reports of oocyte quality and embryo viability are lacking (3, 7).

We present a case of OS and oocyte cryopreservation with subsequent egg thawing and reciprocal IVF cycle with

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anonymous donor sperm in a transgender man who remained on testosterone therapy throughout the stimulation process. The embryo transfer (ET) resulted in a successful clinical pregnancy and live birth.

## CASE REPORT

A 26-year-old transgender man, receiving testosterone therapy for gender affirmation for 4 years, presented for an oocyte cryopreservation cycle with their cisgender female partner. Informed and signed consent was obtained from the couple for the publication of this case report.

The patient was otherwise healthy, with a body mass index of 26.3 kg/m$^2$. His only medication was intramuscular testosterone cypionate 100 mg weekly for 4 years. Baseline ovarian reserve testing was performed before OS. He was comfortable proceeding with transvaginal sonography. Pelvic ultrasound demonstrated a normal uterus and accessible ovaries, with an antral follicle count of 19. Antimüllerian hormone levels (AMH) were not obtained. The patient completed gender-affirming surgery after oocyte cryopreservation.

A gonadotropin-releasing hormone (GnRH) antagonist stimulation protocol was ordered with follitropin alfa (450 IU daily, Gonal-F; EMD Serono, Canada) and lutropin alfa (150 IU daily, Luveris; EMD Serono, Canada). The patient began the GnRH antagonist cetrorelix (Cetrotide; EMD Serono, Canada) on the 5th day of OS, at which point the serum estradiol level was 4,565 pmol/L (1,243.5 pg/mL). Because of the vigorous ovarian response to stimulation with 32 follicles measuring >11 mm in average diameter, a GnRH agonist trigger (3 mg [0.6 mL] leuprolide acetate) was prescribed at 8 PM on the 10th day of stimulation, and the patient was started on oral cabergoline (0.5 mg every 3 days; Dostinex; Pfizer, Canada) for four doses for the prevention of ovarian hyperstimulation syndrome (OHSS). The endometrial thickness measured the day before the trigger was 6.7 mm. Serum testing in the morning before the evening GnRH agonist administration demonstrated a luteinizing hormone (LH) level of 1.9 IU/L and a progesterone level of 11.3 nmol/L (3.3 ng/mL), both of which increased on the day after GnRH agonist administration (12.5 hours after leuprolide acetate injection) to 54.8 IU/L and 39.7 nmol/L (11.5 ng/mL), respectively. This confirmed an acceptable response to the GnRH agonist trigger (10). A transvaginal ultrasound-guided oocyte retrieval was then performed 36 hours after the leuprolide acetate injection.

The egg retrieval was performed under conscious sedation, and 56 cumulous oocyte complexes were retrieved. Twenty-nine metaphase 2 oocytes were cryopreserved through vitrification (17 were germinal vesicles, 7 were metaphase 1, and 3 had degenerated). The patient was monitored for symptoms of OHSS following the procedure and had no complications from treatment.

The couple then presented for a reciprocal IVF cycle using the above-cryopreserved oocytes from 5 years prior. The recipient partner was 31 years old with a normal uterine cavity assessment on a sonohysterogram and ovulatory menstrual cycles. Patient had a cesarean section after donor-sperm insemination with the same donor sperm as used in the IVF cycle.

A hormone replacement ET cycle was prescribed for synchrony with the oocyte thaw, priming the endometrium with estradiol-17$\beta$ 100 $\mu$g dermal patch, 4 patches every 2 days (Estradot, Novartis Pharmaceuticals Canada Inc.), and a transvaginal ultrasound on the 17th day of estrogen priming, confirming a 15.3 mm endometrial thickness. Given an adequate endometrial thickness, intramuscular progesterone in ethyl oleate 50 mg every 3 days with vaginal micronized progesterone 200 mg (Endometrin, Ferring Canada) twice daily was ordered on the 18th day of estrogen priming. Twenty-nine cryopreserved oocytes were then thawed, of which 16 survived the thaw, 13 did not survive the thaw and degenerated. Of the 16 that survived, 12 fertilized with intracytoplasmic sperm injection with the use of anonymous donor sperm (75% fertilization rate). Estrogen and progesterone replacement were continued, and on day 5, fresh ET was performed on a B4–CB blastocyst after protease-assisted hatching. Five embryos met the criteria for cryopreservation at our center (grade B3–BB or better on the basis of the Gardner scoring system) (11).

Twelve days after the ET, a $\beta$-human chorionic gonadotropin of 21 122 IU/L and progesterone of 82.4 nmol/L (23.8 ng/mL) were measured. A follow-up obstetrical ultrasound was performed at 8 weeks gestation by transfer dates, which demonstrated a viable intrauterine pregnancy with a crown-rump length of 18.3 mm (corresponding to 8 weeks and 3 days). The patient has since had a healthy live birth via cesarean section.

## DISCUSSION

Our case is valuable as it adds to the paucity of literature on this important topic and will encourage health care providers to advocate for and refer transgender male patients for fertility preservation. In the above case, an AMH level was not drawn, which would be helpful in future cases given the robust ovarian response despite a modest antral follicle count.

Literature suggests an unpredictable ovarian response in patients on long-term exogenous testosterone. Although the impact of long-term testosterone on ovarian reserve and response is largely unknown, growing evidence suggests the ovaries of transgender men may function and appear histologically similar to those of a patient with polycystic ovary syndrome (12, 13). In 2019, Leung et al. (7) conducted a retrospective cohort study on reproductive outcomes among transgender men and demonstrated a higher number of oocytes retrieved in the transgender male cohort compared with cisgender controls, although the trend was not statistically significant. Androgens are used as add-on therapies to promote follicular response in poor prognosis patients, and it has been proposed that transdermal testosterone may promote ovarian response to recombinant follicle-stimulating hormone and the number and persistence of antral follicles (14–16). Alternatively, testosterone therapy may rapidly suppress AMH levels although it is important to counsel transgender men it does not technically act as a contraceptive (15). Antral follicle counts also do not seem to differ between those who are on testosterone and those who are not at the start of OS cycles (15, 17).

The robust ovarian response may be confounded by the fact that many patients pursue fertility preservation at a young age. This often prompts the need for a GnRH agonist trigger to result in rapid luteolysis and necessitate a freeze-all cycle to reduce the risk of OHSS. There may be concern about the pituitary physiologic response to an agonist trigger after prolonged suppression with testosterone; however, our study center has previously demonstrated a large number of mature oocytes retrieved in a patient receiving prolonged testosterone therapy (18).

In conclusion, informed counseling about continuing testosterone therapy among transgender men seeking fertility preservation should be explored. Our case demonstrated a promising outcome that may allow patients in the future to remain on GAHT, which can encourage patients to seek fertility-based care at an earlier age. More research and, ideally, practice guidelines are needed in this area; however, it is important to note that ovarian reserve markers may be suppressed, ovarian responses may be robust, and oocyte and embryo quality is largely unknown but appears to be reassuring in the limited reports in the literature.

## Declaration of Interests

J.W. has nothing to disclose. A.J. has nothing to disclose. I.D. has nothing to disclose. J.G. has nothing to disclose.

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