Human Reproduction, Vol.38, No.3, pp. 482–488, 2023
Advance Access Publication on January 16, 2023 https://doi.org/10.1093/humrep/dead003

human reproduction

CASE REPORT *Reproductive endocrinology*

Management of testosterone around ovarian stimulation in transmasculine patients: challenging common practices to meet patient needs—2 case reports

Molly B. Moravek [1,*], Marjorie Dixon[2], Samantha M. Pena[2], and Juno Obedin-Maliver[3,4]

[1]Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI, USA [2]Anova Fertility and Reproductive Health, North York, Ontario, Canada [3]Department of Obstetrics and Gynecology, Stanford University School of Medicine, Palo Alto, CA, USA [4]Department of Epidemiology and Population Health, Stanford University School of Medicine, Palo Alto, CA, USA

*Correspondence address. Center for Reproductive Medicine, 475 Market Place, Building 1, Ann Arbor, MI 48108, USA.
E-mail: mpenderg@med.umich.edu https://orcid.org/0000-0001-9972-4938

Submitted on April 15, 2022; resubmitted on December 5, 2022; editorial decision on December 21, 2022

ABSTRACT: Approximately 50% of transmasculine people use testosterone for gender affirmation, yet very little is known about the effects of testosterone on future reproductive capacity. Moreover, there are no data to guide fertility specialists on how to manage testosterone leading up to or during ovarian stimulation. Most clinics require cessation of testosterone prior to ovarian stimulation in this setting of no data; however, the current literature does suggest a potential increase in dysphoria with cessation of testosterone and during stimulation. This divergence begs the question of whether clinicians may be doing more harm than good by enacting this requirement. Here, we present two cases of transmasculine individuals who were on testosterone prior to stimulation and maintained their testosterone dosage throughout stimulation as proof of concept, followed by a discussion of current clinical practice and providing some rationale to support continuation of testosterone throughout stimulation.

Key words: transgender / transmasculine / gender-affirming hormones / testosterone / LGBTQ (lesbian, gay, bisexual, transgender, queer) / ART / ovarian stimulation / fertility preservation / menses

Introduction

In the USA, ∼1.5 million adults, or 0.7% of the population, identify as transgender individuals (people whose gender identity differs from their sex assigned at birth) (Jones, 2022). These numbers can be expected to grow as many studies of youth cite higher proportions of individuals with transgender and non-binary (TGNB) identities, experiences, and expression (1–30%) (Wilson *et al.*, 2017), and recent data note that 1 in 48 Generation Z adults are transgender (Jones, 2022). Further, increasing visibility and socio-political acceptance make disclosure of TGNB identities more common.

Gender affirmation processes (or 'transition') include many actions that help bring one's gender expression (outward appearance) and physiological processes (e.g. hair growth, voice changes, fat distribution, menstrual patterns) into alignment with one's affirmed gender identity. For transmasculine people (individuals who identify as men or on the masculine spectrum and were assigned female sex at birth), these actions include social elements of transition (e.g. changing name, pronouns, driver's license, insurance paperwork, hair, clothes, makeup), medical transition (e.g. using testosterone for masculinization, menstrual suppression), and surgical transition (e.g. chest reconstruction or masculinization—mastectomy, hysterectomy, bilateral salpingo-ophorectomy, vaginectomy, metoidioplasty, scrotoplasty, phalloplasty). As of 2015, in the USA, while 49% of TGNB people assigned female at birth employ testosterone for gender affirmation, far fewer (8% overall) have had a hysterectomy with or without oophorectomy (James *et al.*, 2016). Considering demographic changes, increasing visibility and disclosure, and access to gender-affirming hormones, the number of people of reproductive age on gender-affirming hormones is expected to grow.

Contrary to popular belief, many TGNB people desire to have genetically related children or regret not having that opportunity, and some transmasculine individuals desire to or have carried a pregnancy themselves, even after gender affirmation processes have been initiated (Wierckx *et al.*, 2012; Light *et al.*, 2014; Armuand *et al.*, 2017; Tornello and Bos, 2017; Auer *et al.*, 2018; Chen *et al.*, 2018; Moseson *et al.*, 2021; Vyas *et al.*, 2021). Both national and international organizations have put forth guidelines recommending fertility preservation counseling prior to gender-affirming treatments, including hormone therapy (Ethics Committee of the American Society for Reproductive Medicine, 2015; Hembree *et al.*, 2017; Coleman *et al.*, 2022). Nonetheless, utilization of fertility preservation services remains low among the TGNB population, particularly transmasculine people (Chen *et al.*, 2017; Nahata *et al.*, 2017; Auer *et al.*, 2018; Riggs and Bartholomaeus, 2018). As such, fertility providers will need to grapple with IVF protocols for a subset of transmasculine patients who have already initiated testosterone and are now presenting for fertility treatment in the absence of data-driven practice guidelines. There are published and anecdotal reports of clinics requiring 1–6 months' testosterone cessation prior to IVF, with many clinics requiring the use of oral contraceptive pills or return of menses prior to ovarian stimulation for IVF (De Roo *et al.*, 2016; Armuand *et al.*, 2017; Neblett and Hipp, 2019). Unfortunately, cessation of testosterone often causes 'female-range' serum estradiol levels and return of menses, which can be distressing to transmasculine individuals and increase gender dysphoria (Mitu, 2016; Armuand *et al.*, 2017). Moreover, there is currently no compelling evidence in support of discontinuing testosterone for ovarian stimulation, which begs the question if we could be creating unindicated, unnecessary distress in this patient population by enacting such a requirement. Here, we present two cases of transmasculine individuals who underwent IVF at a single fertility center while continuing gender-affirming testosterone therapy throughout stimulation as a proof of principle, then discuss contemporary practice questions.

Case series

At the fertility center in which the cases described below sought care, transmasculine patients desiring oocyte cryopreservation or IVF are screened for serum anti-Müllerian hormone (AMH) level and antral follicle count (AFC) to inform initial gonadotrophin doses. Gonadotrophins are randomly started without a menses and without stopping or decreasing testosterone therapy. Letrozole 5 mg is administered throughout stimulation to minimize estradiol elevations. GnRH antagonist is started based on follicle size and estradiol levels. Ovulation is triggered with hCG once the lead cohort of follicles reaches 19–21 mm, with oocyte retrieval performed 36 h later. In patients desiring preimplantation genetic testing of embryos, blastocysts are biopsied on Days 5 or 6 of development, and subsequently vitrified for future use. Genetic testing is performed through Access Genomics (Mississauga, Ontario, Canada).

Case 1

A 26-year-old transmasculine individual presented for reciprocal IVF whereby his eggs would be retrieved, fertilized with donor sperm, and embryos transferred to his partner, a cisgender woman. Baseline AMH was 8 ng/ml and AFC was 23. The patient had been on testosterone for 3 years and 8 months prior to ovarian stimulation, with the most recent testosterone level 478 ng/dl. He had a 16-day stimulation with total gonadotrophin dose of 6000 IU and peak serum estradiol 3610 pg/ml. Fourteen oocytes were retrieved, 13 of which were mature. Nine out of 13 mature oocytes successfully fertilized with donor sperm via ICSI, and two embryos developed to the blastocyst stage by Day 5 or 6, at which time they were biopsied and cryopreserved. One of the two blastocysts was reported euploid and successfully transferred to his partner, culminating in a live birth without any pregnancy or neonatal complications.

Case 2

A transmasculine individual who transferred his cryopreserved oocytes from an outside clinic to be fertilized with donor sperm and embryos transferred to his partner, a cisgender woman. He had been on testosterone for 10 years at the time of his ovarian stimulation, which occurred at age 34 years, and he did not stop testosterone during stimulation. His AMH at the time was 9 ng/ml, but we were unfortunately unable to obtain additional details about his ovarian stimulation course. Twenty-three mature cryopreserved oocytes were transferred to the clinic, of which 14 successfully fertilized via ICSI with donor sperm. Eight embryos had developed to the blastocyst stage by Day 5 or 6 and were cryopreserved. No embryos have been transferred to date.

This case series was determined to be exempt from regulation by the University of Michigan Institutional Review Board.

Discussion

While data from case series certainly need to be interpreted with caution, the data presented within this article provide crucial proof-of-concept clinical outcome data from transmasculine individuals who were maintained on testosterone therapy for gender affirmation during ovarian stimulation and suggest acceptable clinical outcomes. While Case 1 had a blastulation rate (28.6%) lower than the clinic's average (53.3%), Case 2 had a blastulation rate of 57.1%, suggesting that the poor blastulation of Case 1 cannot be attributed to testosterone use alone. While the lack of data surrounding the effects of testosterone during ovarian stimulation may be used to justify recommending cessation of testosterone prior to ovarian stimulation, that same lack of data can also be used to justify maintaining testosterone therapy during ovarian stimulation, particularly considering data on increased dysphoria for transmasculine individuals with stopping testosterone and resumption of menses (Armuand *et al.*, 2017).

Impact of testosterone on ovarian function

The impact of exogenous testosterone administration on future reproductive capacity is largely unknown; however, reports of pregnancy in transgender men previously or currently on testosterone provide reassurance that testosterone does not completely eliminate fertility (Light *et al.*, 2014; Moseson *et al.*, 2021). There are also multiple studies that have evaluated testosterone-exposed ovaries at the time of gender-affirming surgery and report changes consistent with polycystic ovarian morphology, but this does not necessarily indicate dysfunction of the

remaining oocytes (Pache et al., 1991; Van den Broecke et al., 2001; Grynberg et al., 2010; Ikeda et al., 2013; Loverro et al., 2016; De Roo et al., 2017). In fact, one case report indicated successful folliculogenesis following FSH stimulation (Van den Broecke et al., 2001) and another reported normal spindle formation in testosterone-exposed oocytes versus controls following IVM (De Roo et al., 2017). In contrast, another study investigating IVM of oocytes obtained from transgender men on testosterone at the time of gender-affirming oophorectomy showed decreased developmental capacity (lower maturation and fertilization rates) compared to donor oocytes from cisgender women (Lierman et al., 2021).

Effect of prior testosterone exposure on IVF outcomes

To date, there have been three case series published on IVF outcomes in transmasculine patients previously on gender-affirming testosterone. In the first study (Adeleye et al., 2019), seven patients who had previously been on testosterone underwent ovarian stimulation. Median testosterone exposure time was 46 months and median time of testosterone discontinuation prior to ovarian stimulation was 6 months (range 1–13 months). They found that, while peak estradiol levels and total oocytes retrieved were lower among transmasculine patients who had previously been on testosterone compared to those who had not, the overall number of mature eggs and maturity rate were not different. Additionally, of the three patients who were pursuing IVF for current fertility, one live birth and one ongoing pregnancy were achieved at the time of publication. In the second study (Leung et al., 2019), 16 transmasculine patients were asked to discontinue testosterone until menses occurred or serum testosterone levels dropped into 'normal' female range. Mean time on testosterone was 44 months and mean discontinuation time prior to stimulation was 4 months (range 1–12 months). Compared to cisgender women, patients previously exposed to testosterone required higher gonadotrophin doses; however, there was no difference reported in oocytes retrieved or mature oocytes obtained. The most recent study (Amir et al., 2020) reports outcomes for six transmasculine people previously on testosterone, all of whom were required to stop testosterone prior to stimulation (range 5–21 months). In this study, the mean (±SD) time of total testosterone exposure prior to discontinuation was 77 ± 55.3 months and, other than higher gonadotrophin requirements, no differences were noted in oocytes retrieved or maturity rates when compared to six transmasculine patients who did not have prior testosterone exposure.

Impact of testosterone exposure during stimulation

There is currently only one published case report on a transgender man who continued testosterone therapy during stimulation. The patient was a 20-year-old transgender man with an 18-month history of testosterone therapy and AMH level 19.6 ng/ml in whom 22 mature oocytes were cryopreserved; however, the quality of those oocytes is, as yet, untested (Gale et al., 2021). In another case report, a 28-year-old transgender man, with a 3-year history of testosterone therapy, serum testosterone 33.3 nmol/l, and AMH level 1.89 ng/ml, had his last testosterone injection 1 week prior to stimulation and was able to cryopreserve 11 mature oocytes (Cho et al., 2020). Although he did not administer testosterone during stimulation, his testosterone serum levels would have presumably still been elevated for all or part of his 13-day stimulation.

Despite a paucity of data on IVF outcomes in transmasculine individuals who remain on testosterone during stimulation, parallels can be drawn with cisgender women with endogenous hyperandrogenism, such as those with polycystic ovary syndrome (PCOS) or congenital adrenal hyperplasia. IVF is an effective means for achieving pregnancy in women with PCOS, even with elevated testosterone and anovulation, although they are at increased risk for ovarian hyperstimulation syndrome (Teede et al., 2018). Additionally, a recent report of IVF outcomes in women with non-classic 21-hydroxylase deficiency (congenital adrenal hyperplasia) showed increasing numbers of viable embryos with increasing testosterone levels, both at baseline and on day of trigger (Jiang and Kuang, 2019). While translation between these clinical scenarios and gender-affirming testosterone must be guarded, because endogenous hyperandrogenism phenotypes are multifactorial with generally lower serum testosterone levels than are targeted in transmasculine individuals, these endogenous conditions provide some initial reassurance that exogenous testosterone does not have a blanket deleterious effect on ovarian stimulation outcomes. Finally, exogenous androgens are actually employed by some fertility clinics to improve outcomes in patients with diminished ovarian reserve, with a recent Cochrane review suggesting testosterone and dehydroepiandrosterone supplementation improve IVF outcomes (Nagels et al., 2015).

Role of menses in timing cycle start

Even if fertility providers are uncomfortable with the idea of continuing testosterone during oocyte stimulation, return of menses should not be required for stimulation. Traditionally, IVF protocols for all patients (regardless of gender identity) have required a natural or induced menses for cycle start, with gonadotrophins for ovarian stimulation commencing on the second or third day of menses. We now know, however, that follicles develop in 'waves' throughout the menstrual cycle, and these follicles can be recruited outside of the follicular phase if exogenous gonadotrophins (FSH, LH) are administered (Baerwald et al., 2003; Sighinolfi et al., 2018). This discovery prompted the proposal of the 'random start' protocol, particularly for cancer patients undergoing time-sensitive fertility preservation, whereby gonadotrophins are initiated regardless of menstrual cycle phase (Cakmak et al., 2013; Sighinolfi et al., 2018). Moreover, the concept of follicular waves led to 'double ovarian stimulation' protocols for poor responders, whereby the patient is stimulated twice in the same menstrual cycle, once in the follicular phase and once in the luteal phase (Ubaldi et al., 2016; Sighinolfi et al., 2018). IVF outcomes—including number of eggs retrieved, fertilization rate, and embryo quality—are similar between 'random start' and traditional IVF protocols, and between follicular and luteal starts in 'double ovarian stimulation' (Cakmak et al., 2013; Ubaldi et al., 2016; Moravek et al., 2018; Sighinolfi et al., 2018). Thus the existing data do not support requiring a (potentially distressing) menses prior to ovarian stimulation in transmasculine patients who do not plan to have an embryo transferred into their uterus. Similarly, there is no reason for administration of the oral contraceptive pill to

time ovarian stimulation, especially since taking such hormones may be incongruent with the patient's gender identity.

For fertility providers who do choose to stop testosterone prior to stimulation, there is no agreed-upon optimal washout period. Some clinicians have argued ~3 months for testosterone washout to allow recruitment of antral follicles that have not developed under testosterone-exposure, taking into account the ~70 days from antral follicle formation to ovulation (Gougeon, 1986); however, this practice only seems logical if there is a proven detrimental effect of testosterone on developing oocytes, which has yet to be established. Others may worry about a potential suppressive effect of long-term testosterone use on the ovary requiring a hormone-free recovery period, similar to that seen in hormonal contraceptive users (Bentzen *et al.*, 2012; Landersoe *et al.*, 2020) but this would likely only apply to patients presenting with a decreased AMH level or AFC. Regardless of washout period, use of progestins or GnRH agonists can be used to prevent dysphoria from the return of menses resulting from testosterone cessation.

Building the evidence base requires comprehensive data

One foundational challenge to providing TGNB patients with evidence-based clinical recommendations is a paucity of data about TGNB people and their health generally, and more specifically information around family building. In part this is due to a long-standing practice, in the USA and around the world, requiring surgical sterilization of individuals as a condition of engaging with gender-affirming care (Dunne, 2017; The Lancet, 2019; lgbtmap.org). Although a sterilization requirement is not officially in place today in the USA, many states require documentation of gender-affirming surgery and/or clinicians' certification to obtain one's driver's license or other critical documentation making this the *de facto* law and thereby limiting activities such as school enrollment, job participation, and other forms of civic engagement (lgbtmap.org). Additionally, TGNB people experience high rates of stigma, discrimination, and violence, even in the healthcare setting, with 33% overall (and much higher for people of color) reporting one or more negative experiences including refusal of care, verbal harassment, providers being physically rough or abusive, and being physically attacked or sexually assaulted in a healthcare setting, which caused more than 23% to delay or avoid care completely (James *et al.*, 2016).

Another reason for the lack of data about TGNB people is missing data and limited population visibility. Healthcare providers, healthcare systems, and research efforts fail to assess and correctly interpret data on comprehensive gender identity and sex assigned at birth, which are necessary to identify and address the health and healthcare needs of TGNB people (James *et al.*, 2016). This failure is despite the 2018 call by Center for Medicare and Medicaid in Meaningful Use three requirements to ensure that all clinical data collection systems are capable of collecting these data (Cahill *et al.*, 2016; AmericanProgress.org). The US National Institutes of Health also recognizes this glaring lack of data, and in 2016 designated sexual and gender minority people as a health disparities population for research (NIMHD). It is therefore incumbent upon providers to assess and document sexual orientation and gender identity.

Additionally, more data are needed comparing outcomes between different protocols on handling testosterone use during ovarian stimulation among people of all genders. Initial studies are already underway in rodent models (Kinnear *et al.*, 2019, 2021), which can hopefully lead to studies in non-human primate models. While randomized controlled trials in humans would obviously be the gold standard for obtaining these data, it would be unethical to randomize transmasculine people owing to the potential dysphoria that can result from testosterone cessation. To this end, a national database of transmasculine individuals undergoing IVF is currently being developed at the University of Michigan to better capture these outcomes. The hope is that such a database can lead to more refined, evidence-based practice guidelines with which hormone providers and fertility providers alike can counsel their patients.

Conclusions and implications for practice and health policy

The medical need for gender-affirming hormones and medical support to have genetically related children should not be mutually exclusive. Given the paucity of knowledge about the effects of long-term testosterone, the best solution for these patients may currently be to make fertility preservation more accessible to patients through insurance coverage prior to starting gender-affirming hormones, consistent with medical guidelines (Hembree *et al.*, 2017; Ethics Committee of the American Society for Reproductive Medicine. Electronic address: ASRM@asrm.org, 2018; Coleman *et al.*, 2022). With financial coverage, fertility preservation could be accomplished without balancing the unknown impact of testosterone. However, even in this 'best' set of conditions, fertility specialists may encounter patients who were not interested, willing, or able to cryopreserve oocytes or embryos prior to starting gender-affirming testosterone.

Reproductive Endocrinology and Infertility specialists have long operated in the realm of minimal clinical data with ultimate patient benefit. For example, advances in IVF and fertility preservation could not have been possible without bold innovation toward meeting patient needs. As such, these specialists should be adept at providing the appropriate counseling and shared decision-making that goes into making reproductive decisions with minimal outcome data. It is important to explore the pros and cons of the decision on whether to stop testosterone prior to ovarian stimulation with the patient, including a discussion of available and extrapolated data from cisgender women and animal models. While it is possible that continuation of testosterone during stimulation may not have as favorable fertility outcomes as stopping testosterone prior to stimulation, for some patients that risk of attenuated fertility outcomes may outweigh the risk of worsened dysphoria with testosterone cessation. In other patients, decreasing the dose of testosterone to match serum levels of cisgender women with hyperandrogenic disorders may represent the most acceptable balance of risk to patients. At a minimum, reassurance can be provided from cases like those presented above that acceptable IVF outcomes, including live births, can be obtained when testosterone is maintained during stimulation. Important to the conversation is the fact that there are currently no data on long-term health of offspring

conceived from testosterone-exposed oocytes. These data are needed.

Regardless of a patient's decision, additional effort should be made to ensure that the clinic environment is a welcoming and safe space for gender diverse patients, and that stimulation protocols minimize worsening dysphoria. Examples include the use of concomitant letrozole with stimulation to minimize estradiol elevations or using transabdominal or pediatric transvaginal ultrasound probes for monitoring in patients with vaginal atrophy or narrowing. However, creating welcoming spaces includes challenging the limits of adopted medical norms and paradigms when they fail to stand up to evidence-based scrutiny and especially if they threaten competing patient health needs. It is our job to meet patients' needs and work with them to weigh family building and gender-affirming goals; providing whole patient care while critically evaluating how regimens may affect all of their goals is critical to supporting our patients now and as future potential parents.

Data availability

The data underlying this article are available in the article.

Authors' roles

M.B.M. and J.O.-M. conceived of the project and design. M.D. and S.M.P. acquired the case data. All four authors contributed to the interpretation of the cases and clinical question, participated in the drafting and/or revision of the manuscript, approved the final version and agree to be accountable to the work.

Funding

M.B.M. was supported by NICHD (R01-HD098233). J.O.-M. was partially supported by NIDDK (K12DK111028).

Conflict of interest

J.O.-M. has consulted for Sage Therapeutics (May 2017) in a 1-day advisory board, Ibis Reproductive Health (a non-for-profit research group; March 2017–May 2018, 2020–present), Folx, Inc. (2020–present), and Hims Inc. (2019–present). The other authors have no conflicts of interest.

References

Adeleye AJ, Cedars MI, Smith J, Mok-Lin E. Ovarian stimulation for fertility preservation or family building in a cohort of transgender men. *J Assist Reprod Genet* 2019;**36**:2155–2161.

Amir H, Yaish I, Samara N, Hasson J, Groutz A, Azem F. Ovarian stimulation outcomes among transgender men compared with fertile cisgender women. *J Assist Reprod Genet* 2020;**37**:2463–2472.

Armuand G, Dhejne C, Olofsson JI, Rodriguez-Wallberg KA. Transgender men's experiences of fertility preservation: a qualitative study. *Hum Reprod* 2017;**32**:383–390.

Auer MK, Fuss J, Nieder TO, Briken P, Biedermann SV, Stalla GK, Beckmann MW, Hildebrandt T. Desire to have children among transgender people in Germany: a cross-sectional multi-center study. *J Sex Med* 2018;**15**:757–767.

Baerwald AR, Adams GP, Pierson RA. Characterization of ovarian follicular wave dynamics in women. *Biol Reprod* 2003;**69**:1023–1031.

Bentzen JG, Forman JL, Pinborg A, Lidegaard Ø, Larsen EC, Friis-Hansen L, Johannsen TH, Nyboe Andersen A. Ovarian reserve parameters: a comparison between users and non-users of hormonal contraception. *Reprod Biomed Online* 2012;**25**:612–619.

Cahill SR, Baker K, Deutsch MB, Keatley J, Makadon HJ. Inclusion of sexual orientation and gender identity in stage 3 meaningful use guidelines: a huge step forward for LGBT health. *LGBT Health* 2016;**3**:100–102.

Cakmak H, Katz A, Cedars MI, Rosen MP. Effective method for emergency fertility preservation: random-start controlled ovarian stimulation. *Fertil Steril* 2013;**100**:1673–1680.

Chen D, Matson M, Macapagal K, Johnson EK, Rosoklija I, Finlayson C, Fisher CB, Mustanski B. Attitudes toward fertility and reproductive health among transgender and gender-nonconforming adolescents. *J Adolesc Health* 2018;**63**:62–68.

Chen D, Simons L, Johnson EK, Lockart BA, Finlayson C. Fertility preservation for transgender adolescents. *J Adolesc Health* 2017;**61**:120–123.

Cho K, Harjee R, Roberts J, Dunne C. Fertility preservation in a transgender man without prolonged discontinuation of testosterone: a case report and literature review. *FS Rep* 2020;**1**:43–47.

Coleman E, Radix AE, Bouman WP, Brown GR, de Vries ALC, Deutsch MB, Ettner R, Fraser L, Goodman M, Green J *et al.* Standards of care for the health of transgender and gender diverse people, version 8. *Int J Transgender Health* 2022;**23**:S1–S259.

De Roo C, Lierman S, Tilleman K, Peynshaert K, Braeckmans K, Caanen M, Lambalk CB, Weyers S, T'Sjoen G, Cornelissen R *et al.* Ovarian tissue cryopreservation in female-to-male transgender people: insights into ovarian histology and physiology after prolonged androgen treatment. *Reprod Biomed Online* 2017;**34**:557–566.

De Roo C, Tilleman K, T'Sjoen G, De Sutter P. Fertility options in transgender people. *Int Rev Psychiatry* 2016;**28**:112–119.

Dunne P. Transgender sterilisation requirements in Europe. *Med Law Rev* 2017;**25**:554–581.

Ethics Committee of the American Society for Reproductive Medicine. Access to fertility services by transgender persons: an Ethics Committee opinion. *Fertil Steril* 2015;**104**:1111–1115.

Ethics Committee of the American Society for Reproductive Medicine. Electronic address: ASRM@asrm.org. Fertility preservation and reproduction in patients facing gonadotoxic therapies: an Ethics Committee opinion. *Fertil Steril* 2018;**110**:380–386.

Gale J, Magee B, Forsyth-Greig A, Visram H, Jackson A. Oocyte cryopreservation in a transgender man on long-term testosterone therapy: a case report. *F S Rep* 2021;**2**:249–251.

Gougeon A. Dynamics of follicular growth in the human: a model from preliminary results. *Hum Reprod* 1986;**1**:81–87.

Grynberg M, Fanchin R, Dubost G, Colau J-C, Brémont-Weil C, Frydman R, Ayoubi J-M. Histology of genital tract and breast tissue after long-term testosterone administration in a female-to-male transsexual population. *Reprod Biomed Online* 2010;**20**:553–558.

Hembree WC, Cohen-Kettenis PT, Gooren L, Hannema SE, Meyer WJ, Murad MH, Rosenthal SM, Safer JD, Tangpricha V, T'Sjoen GG. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2017;**102**:3869–3903.

Ikeda K, Baba T, Noguchi H, Nagasawa K, Endo T, Kiya T, Saito T. Excessive androgen exposure in female-to-male transsexual persons of reproductive age induces hyperplasia of the ovarian cortex and stroma but not polycystic ovary morphology. *Hum Reprod* 2013;**28**:453–461.

James SE, Herman JL, Rankin S, Keisling M, Mottet L, Anafi M. *The Report of the 2015 U.S. Transgender Survey*. Washington, D.C.: National Center for Transgender Equality, 2016.

Jiang S, Kuang Y. The cycle characteristics and outcomes of infertile nonclassic 21-hydroxylase deficiency patients undergoing ovarian stimulation for in vitro fertilization. *Horm Metab Res* 2019;**51**: 315–325.

Jones JM. LGBT Identification in U.S. Ticks Up to 7.1%. *Gallup*. 2022. https://news.gallup.com/poll/389792/lgbt-identification-ticks-up.aspx (17 May 2021, date last accessed).

Kinnear H, Hashim P, Dela Cruz C, Rubenstein G, Chang F, Nimmagadda L, Brunette M, Padmanabhan V, Shikanov A, Moravek M. Reversibility of testosterone-induced acyclicity after testosterone cessation in a transgender mouse model. *FS Sci* 2021: **2**:116–123.

Kinnear HM, Constance ES, David A, Marsh EE, Padmanabhan V, Shikanov A, Moravek MB. A mouse model to investigate the impact of testosterone therapy on reproduction in transgender men. *Hum Reprod* 2019;**34**:2009–2017.

Landersoe SK, Birch Petersen K, Sørensen AL, Larsen EC, Martinussen T, Lunding SA, Kroman MS, Nielsen HS, Nyboe Andersen A. Ovarian reserve markers after discontinuing long-term use of combined oral contraceptives. *Reprod Biomed Online* 2020;**40**:176–186.

Leung A, Sakkas D, Pang S, Thornton K, Resetkova N. Assisted reproductive technology outcomes in female-to-male transgender patients compared with cisgender patients: a new frontier in reproductive medicine. *Fertil Steril* 2019;**112**:858–865.

Lierman S, Tolpe A, De Croo I, De Gheselle S, Defreyne J, Baetens M, Dheedene A, Colman R, Menten B, T'Sjoen G *et al.* Low feasibility of in vitro matured oocytes originating from cumulus complexes found during ovarian tissue preparation at the moment of gender confirmation surgery and during testosterone treatment for fertility preservation in transgender men. *Fertil Steril* 2021;**116**: 1068–1076.

Light AD, Obedin-Maliver J, Sevelius JM, Kerns JL. Transgender men who experienced pregnancy after female-to-male gender transitioning. *Obstet Gynecol* 2014;**124**:1120–1127.

Loverro G, Resta L, Dellino M, Edoardo DN, Cascarano MA, Loverro M, Mastrolia SA. Uterine and ovarian changes during testosterone administration in young female-to-male transsexuals. *Taiwan J Obstet Gynecol* 2016;**55**:686–691.

Mitu K. Transgender reproductive choice and fertility preservation. *AMA J Ethics* 2016;**18**:1119–1125.

Moravek MB, Confino R, Smith KN, Kazer RR, Klock SC, Lawson AK, Gradishar WJ, Pavone ME. Long-term outcomes in cancer patients who did or did not pursue fertility preservation. *Fertil Steril* 2018;**109**:349–355.

Moseson H, Fix L, Hastings J, Stoeffler A, Lunn MR, Flentje A, Lubensky ME, Capriotti MR, Ragosta S, Forsberg H *et al.* Pregnancy intentions and outcomes among transgender, nonbinary, and gender-expansive people assigned female or intersex at birth in the United States: results from a national, quantitative survey. *Int J Transgend Health* 2021;**22**:30–41.

Nagels HE, Rishworth JR, Siristatidis CS, Kroon B. Androgens (dehydroepiandrosterone or testosterone) for women undergoing assisted reproduction. *Cochrane Database Syst Rev* 2015;**11**:CD009749.

Nahata L, Tishelman AC, Caltabellotta NM, Quinn GP. Low fertility preservation utilization among transgender youth. *J Adolesc Health* 2017;**61**:40–44.

Neblett MF, Hipp HS. Fertility considerations in transgender persons. *Endocrinol Metab Clin North Am* 2019;**48**:391–402.

Pache TD, Chadha S, Gooren LJ, Hop WC, Jaarsma KW, Dommerholt HB, Fauser BC. Ovarian morphology in long-term androgen-treated female to male transsexuals. A human model for the study of polycystic ovarian syndrome? *Histopathology* 1991;**19**:445–452.

Riggs DW, Bartholomaeus C. Fertility preservation decision making amongst Australian transgender and non-binary adults. *Reprod Health* 2018;**15**:181.

Sighinolfi G, Sunkara SK, La Marca A. New strategies of ovarian stimulation based on the concept of ovarian follicular waves: from conventional to random and double stimulation. *Reprod Biomed Online* 2018;**37**:489–497.

Teede HJ, Misso ML, Costello MF, Dokras A, Laven J, Moran L, Piltonen T, Norman RJ; International PCOS Network. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Fertil Steril* 2018;**110**:364–379.

The Lancet. Coercive sterilisation of transgender people in Japan. *Lancet* 2019;**393**:1262.

Tornello SL, Bos H. Parenting intentions among transgender individuals. *LGBT Health* 2017;**4**:115–120.

Ubaldi FM, Capalbo A, Vaiarelli A, Cimadomo D, Colamaria S, Alviggi C, Trabucco E, Venturella R, Vajta G, Rienzi L. Follicular versus luteal phase ovarian stimulation during the same menstrual cycle (DuoStim) in a reduced ovarian reserve population results in a similar euploid blastocyst formation rate: new insight in ovarian reserve exploitation. *Fertil Steril* 2016;**105**:1488–1495.e1.

Van den Broecke R, Van der Elst J, Liu J, Hovatta O, Dhont M. The female-to-male transsexual patient: a source of human ovarian cortical tissue for experimental use. *Hum Reprod* 2001;**16**:145–147.

Vyas N, Douglas CR, Mann C, Weimer AK, Quinn MM. Access, barriers, and decisional regret in pursuit of fertility preservation among transgender and gender-diverse individuals. *Fertil Steril* 2021;**115**: 1029–1034.

Wierckx K, Van Caenegem E, Pennings G, Elaut E, Dedecker D, Van de Peer F, Weyers S, De Sutter P, T'Sjoen G. Reproductive wish in transsexual men. *Hum Reprod* 2012;**27**:483–487.

Wilson B, Choi S, Herman J, Becker T, Conron K. *Characteristics and Mental Health of Gender Nonconforming Adolescents in California: Findings from the 2015-2016 California Health Interview Survey*. Los Angeles, CA: The Williams Institute and UCLA Center for Health Policy Research, 2017.

Web references

Identity Document Laws and Policies. *Mov Adv Proj*. https://www.lgbtmap.org/equality-maps/identity_document_laws/name_change (17 May 2021, date last accessed).

STATEMENT: New HHS Rules Require Sexual Orientation and Gender Identity Data Collection in Electronic Health Records Program. https://www.americanprogress.org/press/statement/2015/10/07/122884/statement-new-hhs-rules-require-sexual-orientation-and-gender-identity-data-collection-in-electronic-health-records-program/ (17 May 2021, date last accessed).

Eliseo J, Pérez-Stable MD. Sexual and Gender Minorities Formally Designated as a Health Disparity Population for Research Purposes. https://www.nimhd.nih.gov/about/directors-corner/messages/message_10-06-16.html (17 May 2021, date last accessed).