Marable J, Etcheverry M, Liter B, Wu M. Fertility Options for Transgender Patients: How Can Physicians Provide More Inclusive Care? *Georgetown Medical Review*. 2022;6(1). doi:10.52504/001c.57049

REVIEWS

Fertility Options for Transgender Patients: How Can Physicians Provide More Inclusive Care?

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Keywords: family planning, pregnancy, contraception, transgender care

https://doi.org/10.52504/001c.57049

Georgetown Medical Review

Vol. 6, Issue 1, 2022

Family planning is critical to the sexual and reproductive health of all patients. For transgender individuals, using gender-preferred modalities for conception and prevention can minimize gender incongruence and dysphoria. Currently, the literature describes several pregnancy options including natural conception, gamete cryopreservation, in vitro fertilization, and uterine transplantation. Prevention methods remain similar to those for cisgender patients such as oral contraception, intrauterine devices, condoms, and various surgical procedures. However, great emphasis lies on choosing a method that best supports the chosen gender identity of the patient. This review supports oocyte and sperm cryopreservation as the preferred method for pregnancy and finds consensus with the literature that there is no best method for prevention. As such, physicians should prioritize early discussions with patients and work closely to use modalities that fit each patient's needs and expectations. As the body of literature on LGBTQ+ health continues to grow, this review will help to expand the knowledge around family planning for transgender patients.

Introduction

An estimated 0.5% to 1.3% of the United States population identifies as transgender.[1,2] Family planning remains a complex and multifaceted area within transgender medicine and includes both fertility preservation and pregnancy prevention. While many methods are similar to those for cisgender individuals, physicians should work to ensure treatment options minimize feelings of gender dysphoria, which occurs when one's sex assigned at birth is incongruent with one's current gender identity.[1,3] The current literature reflects a deficit in physician knowledge and training in reproductive health care for transgender patients.[4] Thus, this review explores family planning and barriers to care, as well as clinical implications for health care providers in hopes of increasing accessibility to more inclusive, competent, and evidence-based reproductive medicine.

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Hormone Therapy and Fertility

Many transgender individuals begin hormone therapy to facilitate the development of secondary sex characteristics more congruent with their gender identity. Patients considering hormone therapy should discuss with their physician the long-term effects and fertility implications of treatment.[5] Hormone therapy can have negative impacts on gonadal function and lead to infertility.[6] High testosterone exposure can cause ovarian fibrosis and impaired oocyte release, and high estrogen levels can impair spermatogenesis.[5] Furthermore, some patients may elect to undergo gender-affirmation surgery, such as hysterectomy or penectomy, which are generally considered irreversible.[7] Therefore, fertility preservation is recommended prior to transitional therapy, depending on the goals of the patient. Fertility preservation methods for transgender males include oocyte or ovarian tissue preservation, which can later be used for in vitro fertilization or ovarian tissue transplantation, respectively. Transgender women may undergo fertility preservation with cryopreservation of testicular tissue or semen samples.[5] These interventions may allow patients to explore options such as in vitro fertilization or surrogacy later. There is no standard set of procedures that meets the specific fertility and reproductive needs of all patients. Thus, it is pertinent that health care providers discuss all the reproductive options with patients prior to starting hormone therapy or undergoing surgery.

Fertility of Transgender Men

For many transgender men, fertility and pregnancy are significant concerns. One study reported that 67.4% of transgender women and 61.6% of transgender men had a desire to parent a child, with 50% and 37%, respectively, desiring a biological one.[8] Thus, fertility counseling early in the transition process can aid in attaining these goals. Health care providers should be sure to discuss all options with patients prior to hormone therapy or surgical intervention.[8]

Transgender men can pursue fertility preservation or carry a pregnancy to term before and after gender affirming therapy. However, the effects of prolonged testosterone therapy on pregnancy and fetal outcomes remain unclear. There have been several cases of successful pregnancies in those who have retained female reproductive organs and paused testosterone therapy while pregnant.[9] Testosterone cessation is typically recommended prior to and during pregnancy because females exposed in utero have been found to undergo virilization of their external genitalia.[5] In animal models, long-term health effects of testosterone exposure in utero include delayed puberty, increased aggression, and dysregulation of lipid metabolism in offspring.[10,11] Despite this recommendation, there remains some controversy regarding whether testosterone therapy negatively impacts fetal development.[12] One study reported a developmentally normal 2-year-old child who was born to a transgender man who continued testosterone therapy throughout

pregnancy.[12] This finding suggests that testosterone therapy during pregnancy may not be as harmful as previously believed. Further long-term observation of children exposed to testosterone in utero will be necessary to understanding these effects and updating recommendations.

Testosterone therapy can lead to amenorrhea, which is usually reversible on cessation.[13] The potential to reproduce may be restored soon after cessation of testosterone for those who plan on conceiving. In a study by Light et al,[9] participants who discontinued testosterone to attempt pregnancy reported starting menses again within 6 months, with the majority within 3 months and some even conceiving before the return of menses. Although discontinuation of testosterone may be recommended for a healthy pregnancy, clinicians should be cognizant of the impact that altering hormone therapy may have on patients, including changes in bodily masculinization and exacerbation of gender dysphoria.[14] Proper education on the risks and benefits of treatment can help the patient and provider make an informed decision together.

Oocyte Cryopreservation

There are multiple methods of gamete conservation through fertility preservation for transgender men either prior to gender affirming surgery or on cessation of hormone therapy. Currently, oocyte or embryo cryopreservation is the treatment of choice for most.[13] The procedure begins with controlled oocyte hyperstimulation with gonadotropins, which are used to enhance the maturation of oocytes in vivo.[13,15] On starting the process, patients undergo close monitoring with recurring measurements of serum estradiol and progesterone, as well as frequent transvaginal ultrasounds to monitor follicular growth. Approximately 10 to 14 days later, oocytes are retrieved via aspiration of the transvaginal follicular fluid. The collected oocytes are subsequently isolated, and the mature oocytes are cryopreserved. With embryo cryopreservation, mature oocytes are either conventionally fertilized by introducing motile sperm into the culture or via intracytoplasmic injection, in which sperm is directly injected into the oocyte.[13,15]

Ovarian Tissue Cryopreservation

When oocyte or embryo cryopreservation is not feasible, ovarian tissue cryopreservation is a promising experimental procedure that can be performed at the same time as gender-affirmation surgery without the need for ovarian stimulation or gynecologic examination.[13] It is currently the only available option for prepubertal transgender males. Ovarian tissue cryopreservation is typically offered to prepubertal patients diagnosed as having cancer who must be treated with gonadotoxic therapy or oophorectomy.[15-17] The procedure begins with a laparoscopic biopsy of the ovarian cortex because it contains a large number of follicles, followed by cryopreservation, thawing, and eventual use of gametes through tissue reimplantation. Ovarian function can last up to 7 years post transplantation.[15] Despite these potential benefits and successes, reimplantation of tissue in transgender men can lead to undesirable female

hormone production. To circumvent this, a novel technique called in vitro maturation that involves activating and maturing immature oocytes from cryopreserved tissue outside of the body has gained traction.[13,15-17] This technique shows great potential to achieve in vitro fertilization without tissue reimplantation.

Fertility of Transgender Women

Transgender women have several options for fertility preservation. Fertility methods are best sought before any hormone therapy or surgery because antiandrogen and feminization treatments impair sperm quality and quantity.[18] Furthermore, it remains unclear how long hormone treatments need to be stopped before testicular histology and spermatogenesis return to normal, as high heterogeneity in testicular histology, irrespective of the treatment strategy, has been reported.[3] Further studies can help to investigate this phenomenon and provide clinical insight.

Sperm Cryopreservation

Sperm cryopreservation is the standard fertility preservation protocol. Sperm are frozen for storage and thawed at the time of use.[19] Specimens are typically obtained via masturbation; however, some individuals may find the act of ejaculation as inherently male, causing psychological distress.[13] Surgical sperm retrieval is an alternative method that can help alleviate this. Surgical sperm retrieval involves retrieving sperm directly from parts of the testis or epididymis and can be performed at the time of gender affirming surgery.[13] Testicular tissue cryopreservation to grow and mature sperm in vitro may also be an option in the future for transgender men; however, it is currently only available to prepubertal boys undergoing cancer treatment where spermatogenesis is still immature.[13,20]

Uterine Transplantation

Uterine transplantation has become a promising development in fertility preservation for transgender women. To date, uterine transplantations are experimental and have only been successfully performed in cisgender women to restore fertility.[21-23] In 2020, there were at least 70 uterine transplantations performed worldwide with the delivery of 20 healthy infants.[24] In contrast to traditional solid organ transplants, uterine transplants are used only for a limited number of years and are eventually removed, allowing for the discontinuation of any immunosuppressive medications. In a study surveying 182 transgender women, nearly all respondents (99%) believed uterine transplantation would lead to greater happiness, which suggests the procedure may address their fertility and reproductive goals while alleviating gender dysphoria.[21] However, there are several anatomical complexities to consider, including vascular and neovaginal anastomoses, pelvic size and shape, and the absence of vaginal mucosa in transgender women.[21,25] Over the last few decades, uterine transplantation has become an innovative method for fertility

restoration in otherwise infertile women.[21-23] Further research in needed on the potential physiologic and psychosocial implications of this procedure. However, uterine transplantation could provide many transgender women the opportunity to conceive their own children and is a promising advancement in transgender medicine.[21-24]

Pregnancy Prevention

Pregnancy prevention is an integral component of family planning. While pregnancy and parenthood may be a desire for some individuals, the knowledge and ability to prevent unwanted pregnancy are similarly important.

Common Myths

Counseling on contraceptive methods for transgender patients differs depending on the gender affirming therapies that they may have previously undergone. Transgender men who have not had a hysterectomy or salpingectomy may still be able to become pregnant, even if they are taking testosterone and are amenorrheic.[26] Testosterone is not an appropriate form of contraception. Between 16.4% and 31% of transgender men believe that testosterone is an effective contraceptive and 5.5% to 9% of these individuals received this information from a health care provider.[4] Additionally, 54% of transgender men taking testosterone discontinued their contraceptive once they became amenorrheic, underscoring the importance of education surrounding contraception use with concomitant testosterone therapy.[27] Transgender men experience rates of unintended pregnancy similar to cisgender women in the United States, indicating the need for counseling on the prevention of pregnancy in this population.[26]

Methods of Pregnancy Prevention

Pregnancy prevention methods focus primarily on individuals with uteruses. Testosterone is not a known contraindication for any form of contraception currently available for individuals with uteruses; therefore, transgender men should be made aware of all their options.[4] Differences in contraception use have been reported between transgender men and cisgender women, with the former favoring methods that suppress menstruation.[4] When counseling transgender individuals on pregnancy prevention, special considerations must be taken to minimize gender dysphoria associated with contraceptive use.[4]

The first step for pregnancy prevention counseling should be to assess the desire for future pregnancy. If the patient expresses no desire to ever become pregnant, the patient should be counseled for permanent methods of contraception, including a hysterectomy and/or oophorectomy.[4,28] Transgender men may want to avoid hormonal birth control, due to its association with cisgender women and/or the thought of feminization of their bodies due to estrogen and progesterone.[4] However, studies have shown that the level of estradiol in the oral contraceptive pill is not high enough to reverse or prevent the masculinizing effects of testosterone and that testosterone levels

remain within the anticipated range in transgender men using an estrogen-based oral contraceptive pill.[4,29] In a study of transgender men receiving testosterone therapy, those using estrogen and/or progesterone-based birth control methods had a mean testosterone level of 548.6 ng/dL ± 325.8 (95% CI, 460.8-638.6).[29] Additionally, transgender men may have concerns about contraceptive methods that require pelvic procedures, such as an intrauterine device (IUD), and methods that increase chest tenderness, because these may be significant causes of gender dysphoria.[4] However, the levonorgestrel IUD may be favorable for some transgender men due to its effects on decreasing the length of endometrial bleeding and pelvic cramping, as well as the potential for amenorrhea.[26] Because testosterone therapy may not always stop menstruation, the levonorgestrel IUD may be a desirable option. Alternatively, the copper IUD may be preferred by patients who want to avoid hormonal contraception.[4,5] Physicians should discuss all prevention options to best fit the needs and goals of their patient.

Transgender women should be counseled on pregnancy prevention congruent with their current anatomy and potential to produce sperm, if having sex with a partner(s) in which a pregnancy could result. Prevention methods are primarily focused on cisgender women and transgender men, indicating a notable gap in current guidelines.

Clinical Implications

The transgender community remains a marginalized group in medicine. Understanding both the fertility and pregnancy prevention options is critical for physicians to provide quality care. This section will explore clinical implications and outline the importance of providers having a strong understanding of transgender medicine.

Transgender patients frequently encounter significant barriers to seeking care. Patients have reported stigma, providers with inadequate knowledge about transgender health, discrimination, and misgendering due to transphobia as negative influencers to seeking care.[30] Physicians should work to educate themselves to better understand the specific concerns of this community. This is especially important for patients who experience gender dysphoria. While understanding that puberty blockers, such as leuprolide, can have negative effects on bone development and density is critical, it is important to know that the emotional relief provided by these may outweigh the negative adverse effects. Moreover, it was found that using language such as “endometrial bleeding” rather than traditional feminine phrases such as “menstrual bleeding” or “period” can cause less dysphoria in transgender men.[5] Providers carry this responsibility to adapt their traditional lexicon to create safer and more inclusive spaces for their patients. Providers, especially pediatricians and adolescent medicine clinicians, should also be aware of the physical changes that transitional hormones cause.[5] For example, following initiation of testosterone therapy, clitoral enlargement, amenorrhea, and vaginal dryness

and atrophy are expected. To provide the best possible care for the transgender community, providers should work to create a welcoming and inclusive environment, thus increasing accessibility and the likelihood of service utilization.[5] Overall, understanding the patient population will allow providers to address patient concerns and provide better care.

Family planning is a mainstay of reproductive health. Many transgender men and women express the desire to begin a family, and family planning proves to be a valuable option for couples who wish for biological children. Currently, the most effective options are sperm and oocyte and/or embryo cryopreservation.[7] This requires thoughtful and early conversations around family planning. Physicians should carefully and thoroughly discuss with patients the options and explain the potential risks and outcomes. The European Society of Human Reproduction and Embryology recommends providers do so prior to beginning hormone therapy due to the impacts of testosterone on embryo development and estrogen on sperm quality.[8,12,18] Having these discussions prior to commencement of hormone therapy can also prevent the discontinuation of transitional hormones, which can be emotionally damaging and exacerbate gender dysphoria.[12] Even with insurance coverage, fertility preservation options remain expensive, so providers should be sure to explain all the options to patients.[6]

Appropriate contraceptive use and patient education is critical to the effective prevention of pregnancy. For many transgender patients, pregnancy is unwanted and even a source of gender dysphoria. Physicians should talk with their patients about fertility prior to starting the transition process if possible.[8] Because many of the contraceptive options, such as estrogen and progesterone birth control, can exacerbate feelings of dysphoria, a thorough discussion of options is essential. While testosterone may help patients achieve amenorrhea, it is not a form of birth control.[31] However, for those who have reached amenorrhea while taking testosterone, a copper IUD may be an effective alternative to the hormonal IUD.[5] Last, physicians should be prepared to discuss safe abortion options to minimize unsafe methods. In a national survey of transgender adults, more than 1 in 3 respondents had considered ending their pregnancy on their own, and nearly 1 in 5 attempted to do so.[30] These attempts included physical trauma as well as substance and drug abuse. Providers should strive to educate their patients to prevent dangerous and unsupervised abortions. In addition, abortion clinics should work to improve inclusivity, including writing "individuals" rather than "women" on their forms.[30] Promoting safer prevention and abortion methods is key to protecting all patients.

Conclusions

This review demonstrates that pregnancy and fertility preservation are realistic options for certain transgender individuals. Thus, educating patients and providers in this area of medicine will significantly improve transgender health

care. For transgender men, natural conception is a possible method for having children. With provider guidance and updated recommendations on testosterone therapy and its potential effects, transgender men can deliver healthy infants. Additionally, there is hope for conception in transgender women with advances in uterine transplantation. Fertility preservation also allows for both transgender men and women to conserve gametes and reproductive tissue. This provides significant patient autonomy in the family planning process and allows for individuals to become parents when they decide to do so.

With advances in reproductive options for transgender patients, it is vital to educate and empower individuals regarding their reproductive potential and provide resources for contraception if pregnancy is undesired. It is important to discuss that there are various contraceptive options available, and each may affect individuals differently. Thus, proper counseling can improve the health and well-being of each patient. Last, providers have a responsibility to educate themselves in transgender medicine to increase accessibility and inclusivity for patients. Providers who understand the delicate intricacies of transgender fertility and understand the importance of early discussions around pregnancy may prove to be invaluable resources for patients and their fertility needs.

Understanding the relevance, risks, and timeline in care for transgender patients is essential to supporting them and their reproductive health. Greater sensitivity, increased knowledge, and early conversations are fundamental to ensuring the best fertility care possible. While the literature demonstrates positive advancements in transgender reproductive health care, greater focus on educating physicians not only on fertility options, but also the psychosocial implications is needed to ensure that all transgender patients have access to competent and compassionate care.

Conflicts of Interest

The authors declare no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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