

Fertility Preservation Outcomes and Considerations in Transgender and Gender-Diverse Youth

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Transgender and gender-diverse adolescents and young adults (TGD-AYA) increasingly present to health care providers seeking medical affirming interventions (MAIs) to induce physiologic changes aligned with their gender identity. MAIs include gonadotropin-releasing hormone agonists to temporarily suppress puberty, testosterone to induce masculine characteristics among those assigned female at birth, and estrogen (often combined with an antiandrogenic agent) to induce feminine characteristics among those assigned male at birth. There is considerable concern that these MAIs impact gonadal structures and function, thereby decreasing future fertility potential.¹ Little research has explored reversibility or thresholds (amount and/or duration) of MAIs in impacting TGD-AYA fertility. Therefore, multiple professional organizations recommend fertility counseling before MAI initiation.²⁻⁴

In this month's issue of *Pediatrics*, Barnard et al⁵ provide the first study of semen cryopreservation outcomes among TGD-AYA assigned male at birth who assert a female gender identity. They conducted retrospective chart reviews on 11 TGD-AYA referred for fertility preservation over a nearly 4-year period. One patient did not provide a sample. The 8 samples obtained from patients before MAI initiation were all viable. One patient who was on gonadotropin-releasing hormone agonists for 6 months before

semen collection had a low-quality sample 3 month after discontinuation, but 2 months later, a viable sample was obtained. Another patient on estrogen and an antiandrogenic agent (spironolactone) for 26 months was unsuccessful in producing sperm for 4 months after discontinuation leading up to scheduled orchiectomy.

Barnard et al⁵ recognize the limited generalizability due to small sample size, particularly having only 2 patients who provided samples after starting MAI. Confounding factors, such as smoking, obesity, or psychological stress, could also prevent normal samples from being obtained. Stress is a relevant factor for TGD-AYA because stopping MAI may increase gender dysphoria or result in greater self-awareness of potential stigma or rejection by others. Secondly, the course for the single patient on estradiol and spironolactone was limited by orchiectomy. It cannot be assumed that a viable sample could not be obtained with more time or that this supports any association between MAI and permanent infertility. Studies of transgender adults, as reviewed by Barnard et al,⁵ demonstrate normal sample collection after starting MAI.

Semen cryopreservation outcomes before MAI are expected to follow trends for age-matched peers. Similar successful outcomes have been shown among adolescents with cancer after pubertal onset but before gonadotoxic treatments.⁶ Barnard et al⁵ demonstrate that collection before MAI

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is quick and effective, which is important in preventing gender dysphoria caused by later discontinuation of MAI for a considerable time and multiple collection attempts. There is often urgency to start MAI among TGD-AYA due to gender dysphoria and related psychological sequelae. However, starting MAI immediately and delaying fertility services may lead to increased overall morbidity for some patients.

The standard of providing fertility counseling before MAI does not always occur. In 1 study of 158 TGD-AYA, only 20% reported discussing fertility, and 13% reported discussing effects of MAIs on fertility. Meanwhile, 60% expressed interest in learning more.⁷ One limiting factor is the lack of practice guidelines and studies to guide physicians in providing effective fertility counseling to TGD-AYA.

Barnard et al⁵ review data suggesting TGD-AYA have low interest in fertility services, but many TGD-AYA questioned whether this may later change.⁸ Among adult transgender populations, interest in biological children is the same as that of age-matched peers.⁹ After starting MAIs, TGD-AYA report being more emotionally capable of considering future parenting because of increasing comfort with their bodies and romantic relationships.¹ Developmentally, adolescents focus on personal identity and orient toward the present over future desires or consequences. This makes fertility counseling and family planning challenging, especially when disagreeing perspectives arise between adolescents and parents. Family and individual therapy can help in exploring values and perspective taking. Tools are also available to help TGD-AYA and guardians explore attitudes toward fertility, including the Transgender Youth Fertility Attitudes Questionnaire.⁸

TGD-AYA use of fertility services is also low.^{1,9,10} The high cost is a consideration because such services often are not covered by insurance, and pursuing them requires financial resources up front. Other barriers include low availability of services, collection procedures causing dysphoria, and desire not to delay MAIs.^{1,9} Stereotypes and stigma contribute, such as assuming one's identity dictates an inability or decision not to reproduce. Under a reproductive justice framework, autonomy around family planning is a right that should not be limited by structural or systemic barriers.¹¹ Many professional organizations, including the American Academy of Pediatrics, advocate for access to essential health care by TGD-AYA, which includes fertility services.¹²

Overall, there is a clinical and ethical imperative to better understand and provide access to fertility services for TGD-AYA. Barnard et al⁵ pave the way, but more research is critical to characterize the potential for and limitations of fertility preservation, specifically after initiating MAIs, and on alternative approaches that are more effective and/or better tolerated.

ABBREVIATIONS

MAI: medical affirming intervention

TGD-AYA: transgender and gender-diverse adolescents and young adults

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