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3 groups based on discontinuation of estrogen at 2 weeks, 6 weeks prior to procedure or not at all. There was no significant difference in spermatogenesis in the different groups despite higher serum and intratesticular testosterone levels in those that stopped the estrogen. The important take home message here is that despite estrogen therapy, some transgender females will continue to undergo spermatogenesis. Size matters; as smaller testes had a much lower chance of finding spermatogenesis than normal sized testes which is not the case in most cases of nonobstructive azoospermia. One must think of these patients to be similar to oncologic patients where this is the last time that biologic sperm will be available to them to cryopreserve. Even at the late stage of gender affirming surgery, testis sperm extraction ex vivo at time of orchiectomy should be offered to all patients undergoing bilateral orchiectomy with or without vaginoplasty to preserve sperm for future use.

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EDITORIAL COMMENT



This article highlights the importance of fertility preservation prior to gender affirming surgery which ideally should be done prior to initiation of hormone therapy. This is critical to the preoperative care of the transgender person who wishes to undergo surgery. The World Professional Association for Transgender Health recommends discussion of fertility prior to the initiation of treatment and prior to any fertility affecting surgery.¹ Estrogen appears to have an incomplete deleterious effect on spermatogenesis. Adeleye et al reported that patients on estrogen therapy still had low levels of sperm in their ejaculate (mean total motile 0.2million/cc).² The authors of the current study here report that of the 72 patients on hormone therapy for a median of 39 months who underwent bilateral orchiectomy with or without vaginoplasty, 81% still had germ cells present and 40% had evidence of elongated spermatids present on histologic evaluation. There was no statistically significant difference in age or time on hormone therapy in presence of some full sperm maturation noted on histologic evaluation. The most important factor identified in this paper was that in testes less than 10 mL, only 9% had elongated spermatids, and this increased to 85% in testes >25 mL.

So why do some patients on estrogen and other antiandrogens such as spironolactone still have spermatogenesis, while others do not? It may be a function of compliance of estrogen therapy, dosage of estrogen or effects of the antiandrogens. Schneider et al reviewed³ their data in a similar population. They evaluated

AUTHOR REPLY

The search for reliable fertility preservation options for transgender women is ongoing. It is not clear which patients on long-term estrogen and other antiandrogens have preserved spermatogenesis. Our research may lead to hope for these individuals as we found evidence of spermatogenesis in 40% of orchiectomy specimens. Our data suggest that patients with preserved testicular size are the best candidates for successful sperm retrieval, though all patients should be counseled that such efforts at fertility preservation remain investigational. We agree that patients undergoing orchiectomy as part of gender-affirming surgery should be offered ex vivo sperm extraction.

Ideally, cryopreservation of semen should be done prior to initiation of hormone therapy; however, with the increasing popularity of pubertal suppression for transgender children, this may become a vanishing option.¹ The current Holy Grail of fertility preservation research lies in the successful culture and differentiation of spermatogonial stem cells. This is an active area of basic science research with meaningful recent advancements in the animal world.^{2,3} In vitro culture of human spermatogonia has proven challenging, as has in vivo maturation of human spermatogonia in xenografted cryopreserved immature testicular tissue.^{4,5} Despite these challenges, if cryopreserved human tissue can be matured later to produce viable sperm, this would not only impact



transgender fertility preservation but also pediatric oncofertility and multiple instances of nonobstructive azoospermia.

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