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The role of androgens on the clitorophallus and possible applications to transgender patients

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Abstract

Background: The clitorophallus, or glans, is a critical structure in sexual development and plays an important role in how gender is conceptualized across the lifespan. This can be seen in both the evaluation and treatment of intersex individuals and the use of gender-affirming masculinizing therapies to help those born with a clitoris (small clitorophallus with separate urethra) enlarge or alter the function of that structure .

Objectives: To review the role of testosterone in clitorophallus development from embryo to adulthood, including how exogenous testosterone is used to stimulate clitorophallus enlargement in masculinizing gender-affirming therapy.

Materials and Methods: Relevant English language literature was identified and evaluated for data regarding clitorophallus development in endosex and intersex individuals as well as the utilization of hormonal and surgical masculinizing therapies on the clitorophallus. Studies included evaluated the spectrum of terms regarding the clitorophallus (genital tubercle, clitoris, micropenis, penis).

Results: Endogenous testosterone, and its more active metabolite dihydrotestosterone, play an important role in the development of the genital tubercle into the clitorophallus, primarily during the prenatal and early postnatal periods and then again during puberty. Androgens contribute to not only growth but also the inclusion of a urethra on the ventral aspect. Exogenous testosterone can be used to enlarge the small clitorophallus (clitoris or micropenis) as part of both intersex and gender-affirming care (in transmasculine patients, up to 2cm of additional growth). Where testosterone is insufficient to provide the degree of masculinization desired, surgical options including phalloplasty and metoidioplasty are available.

Discussion and Conclusion: Endogenous testosterone plays an important role in clitorophallus development, and there are circumstances where exogenous testosterone may be useful for masculinization. Surgical options may also help some patients reach their personal goals. As

masculinizing gender-affirming care advances, the options available for clitorophallus modifications will likely continue to expand and improve.

Introduction

At the time of birth, one anatomic structure has historically been central to the immediate postnatal determination of sex (and for many decades, gender). The size of this structure on prenatal ultrasounds may lead parents to hypothesize elements of their future child's life course as well as decision making around everything from names to room color.[1,2] Alteration of this structure is central to religious identity for some individuals and deeply offensive to others.[3–5] This structure is the clitorophallus (Table 1).

The clitorophallus is most often referred to as either a penis or clitoris. This reflects the two most common developmental pathways, typically referred to as male and female. Clitorophallus size, the presence of other genital structures (e.g., vagina, scrotum), and the location of the urethra often dictate whether the clitorophallus is referred to as a penis (enlarged, with urethra present to tip) or a clitoris (small, urethra separate). However, requiring the clitorophallus to be categorized as either a penis or clitoris masks the range of variation seen in normal human development. Some persons have a larger clitorophallus with a discretely separate urethra or have a proximal and/or ventral urethra (e.g., hypospadias).

When there is a variation in the size or structure of the clitorophallus that makes categorization difficult, it is often referred to as an intersex trait or difference in sexual differentiation. Many such variations are non-pathologic and do not require acute intervention, and defaulting to a binary language of clitoris or phallus limits the understanding of the diversity of this structure's anatomic size and function.[6] For example, a baby born with a prominent clitorophallus that has a urethral opening at the base might be documented as having a "micropenis with hypospadias" or an "enlarged clitoris." Both are linguistically and clinically correct, and yet each has specific gendered outcomes attached. If the infant is labeled as having an enlarged clitoris , they will likely be said to be presumptively female sex, unless proven otherwise, and both clinical care and parental education will be provided with that foundation. Alternatively, if an infant is labeled as having a micropenis with hypospadias, they will likely be presumed to be male, and clinical counseling will prioritize viewing this structure as a penis in need of modifications.

Defaulting to language that forces a spectrum of clitorophallus development into binary options limits the ability of parents, patients, and providers to understand the functionality and diversity of this androgen-sensitive structure, particularly in the context of anatomical (intersex) and gender diversity. There is growing evidence that using the size and structure of the clitorophallus to assign gender and sex can be problematic, as sex and gender are not the same in all persons and sex is not a binary state.[7–9] Some people with a small clitorophallus may desire a larger one and vice versa, but sex is not the only predictor of that goal. Individual assessment of and goals for the clitorophallus also reflect gender identity, functional desires, perceptions of normality, medicalization, and cultural influence.[6,10] To explicitly recognize the developmental diversity of the postnatal structure which develops from the genital tubercle in utero, this study will utilize the term clitorophallus, unless specifically referencing another study's data (In practice, clinicians and researchers should routinely ask individuals to share their preferred terms for any relevant aspects of their anatomy and use those terms throughout the visit.).

Despite the clitorophallus' central role in many of life's milestones and intimate relationships, it is typically an aside or afterthought in discussions of the effects of androgens on the body. Most literature on the clitorophallus surrounds early medical and surgical interventions used to address structural variations, including hypospadias and micropenis. Other research takes places in context of gender affirming care, where those who are born with a small clitorophallus and separate urethra may desire to enlarge this structure as a part of masculinization therapies.[11]

As our understanding as clinicians improves regarding the nature of sex and gender diversity it is time to revisit the clitorophallus and understand its origins, development and modifications and the central role androgens play at each stage thereof. This paper will review the role of testosterone in clitorophallus development from embryo to adulthood, including how exogenous testosterone is used to stimulate clitorophallus enlargement in masculinizing gender affirming therapy. To do this, relevant English language literature was identified and evaluated for data regarding clitorophallus development in endosex and intersex individuals as well as the utilization of hormonal and surgical masculinizing therapies on the clitorophallus. Studies included evaluated the spectrum of terms regarding the clitorophallus (genital tubercle, clitoris, micro-penis, penis).

Prenatal Development of the Clitorophallus

In early fetal development a limb bud forms made up of endoderm (the cloacal extension for the urethral plate), mesoderm, and ectoderm and becomes the genital tubercle.[12] The genital tubercle is a projection from within the perineum and exists in many species.[13] Unlike other limb development in the human fetal body, the understanding of the genital tubercle development still lags behind.[12] The human genital tubercle has a range of developmental potential ranging from small to large, containing a urethra or not, irrespective of genotype.[14]

The initial development of the genital tubercle is androgen independent, as it begins to form prior to the synthesis of fetal androgens (in the gonads or adrenals). [13] The structure is first recognized at 5 to 6 weeks of development. [13] The fetus does not start to synthesize androgens until between 8 and 10 weeks, and prior to 10 weeks, the genital tubercle is identical in size and morphology across all individuals. [13] From 9 weeks to 12 weeks the orientation of the tubercle will change. In a more androgenic environment, the structure will orient 90 degrees to the perineum, where those in a hypoandrogenic environment will remain parallel. [13] It is not until 12 weeks where an androgen responsive and exposed genital tubercle grows larger than a structure that is either not exposed to androgens or not responsive (androgen insensitive).[14]

The embryologic endpoint of the genital tubercle is the clitorophallus, which contains several homologous structures, regardless of developmental pathway. The corporal bodies are a fusion of the crura which are attached proximally to the inferior pubic rami. [13] They contain sinusoidal erectile tissue surrounded by the tunica albuginea and are present prior to the presence of androgens.[14] All clitorophallus also contain a glans, where the initial formation is androgen independent. Along the shaft of the clitorophallus are nerve bundles which run along the corporeal bodies, the densest of which are just lateral to the midline dorsal arteriovenous bundle, on either side of it.[14] Nerve branches extend up to the glans and around the tunica albugenia.

A fully differentiated (morphologic changes in response to hormones and development) clitorophallus is typically seen by 16-17 weeks. [15] The ends of the possible developmental spectrum are the sexually dimorphic clitoris (small clitorophallus, separate urethra) and penis (large

clitorophallus, contained urethra). However, due to gradients of androgen exposure, androgen sensitivity, and other developmental concerns, the clitorophallus can end up anywhere along the spectra of size and urethral location. These morphologic variants are collectively termed intersex variations or differences of sexual development. [12] There are, however, no clear guidelines as to what constitutes a clitoris, what constitutes a penis, and what lies in between. A substantial fraction of classification relies upon the associated genitalia and clinicians involved (e.g., a large clitorophallus in someone with a vagina may be termed a hypertrophic clitoris and a small clitorophallus in the absence of vaginal opening with urethra contained may be termed a microphallus).[16] For the purpose of better describing the developmental spectrum of the clitorophallus, we will describe the developmental pathways most commonly seen under conditions of full androgenic exposure, partial androgenic exposure, and little to no androgen exposure.

Androgen exposure is dependent both on the levels of androgens in the fetal environment and on the presence of functional androgen receptors. From 9-16 weeks, androgen receptors (AR) are prominent throughout the clitorophallus, particularly in the corporeal body, and ventral mesenchyme. In those without high androgen exposure, AR are not seen in the area of the mesenchyme where an androgenized urethral plate would otherwise develop.[15]

Estrogen receptor alpha (ERalpha) and beta (ERbeta) are also expressed during this developmental period, though less prominently so.[15] Despite early theories that androgens were the sole determinator of clitorophallus growth and development, ERalpha has also been found to influence development.[12] In mice, ERalpha has been implicated as acting in opposition to the virilization potential of androgens in the clitorophallus, as ERalpha mutation models lead to a virialized clitorphallus.[17] Elevated estrogen exposure during early pregnancy in mouse models will also result in under-virialized clitorophallus.[17] This suggests estrogen receptor activity is necessary for the inhibition of growth.[12] Progesterone receptors are never seen in the embryologic development of the clitorophallus.[15]

Prenatal Clitorophallus Development under Full Androgen Exposure

In those with functional testes and AR, testicular androgens increase significantly after the 8-10 week period. [1314,18] At 8-9 weeks of gestation, leydig cells in the newly formed testes will begin to

form testosterone. This causes the clitorophallus, particularly the corpora cavernosa, to enlarge. In a fully androgen exposed fetus the clitorophallus will also typically have a urethra contained on the ventral aspect (see urethral plate, below).

Testosterone, and its more potent metabolite dihydrotestosterone (DHT), are responsible for growth and development of the genital tubercle into a larger clitorophallus. [14] DHT is converted from testosterone by 5-alpha reductase 2 (5aR2), and both 5aR2 and AR are present in the mesenchymal and epithelial cells of the genital tubercle.[19] The genital tubercle also has the ability to synthesize DHT from a testosterone-independent pathway [19]

While the primary pathway of androgens for virilization arises from the testes, the alternative "backdoor" production pathway of androgens in the adrenal glands is also thought to be necessary for virilization of a clitorophallus.[20] Although this production is small in comparison to production within functional testes, it can play a more significant role in individuals with partial androgen exposure[20]

Prenatal Clitorophallus Development under No Androgen Exposure

In persons with minimal to no androgens (including those with AR defects such as complete androgen insensitivity), the genital tubercle will still elongate slightly.[18] It will otherwise remain as a small glans with a short shaft and a separate urethra (see urethral plate, below). The clitorophallus will remain parallel to the body wall.[13]

Prenatal Clitorophallus Development under Partial Androgen Exposure

When the genital tubercle is exposed to some androgens or has defects in the AR (such as partial androgen insensitivity or 5aR2 deficiency), variations in clitorophallus anatomy can occur. The type of variation in androgen exposure typically influences the degree of virilization. In those who have a defective 5aR2 gene, the clitorophallus does not virialize greatly, suggesting DHT is critical to this process.[12,19] Fetuses with AR defects do not exhibit growth of the clitorophallus or incorporation of the urethra to the same degree as those with intact receptors. [13]

In some patients who have no testicular androgens, they will have virilization greater than anticipated due to virilization from the adrenal pathway or exposure to maternally produced androgens.[20–22] In congenital adrenal hyperplasia (CAH) the adrenal pathway can produce significant androgens, leading to clitorophallus growth. Clitorophallus morphology of a typical penis can be seen in severe hyperandrogenic CAH patients, suggesting the degree of androgen exposure is related to the degree of morphologic change. [13]

Prenatal Urethral Plate Development

Urethral plate development is incompletely understood but thought to be related to endodermal cloacal epithelium, as described in mammals.[13] It begins at 9-10 weeks' gestation. This early process is considered androgen independent as it occurs in both sexes. However the folding of the urethral plate into a tube, which then canalizes into the clitorophallus, occurs around the time that testosterone is elevated in an androgen exposed fetus and is considered to be androgen dependent. [14] AR are in both the epithelium and mesenchyme of urethral and vestibular folds of all fetuses, and ERbeta is found in the urethral plate prior to differentiation.[15] In a full androgen environment, the urethra will typically extend to the tip of the glans; however, variations in this anatomy can occur as in hypospadias. In cases where the hormonal environment is not dominated by androgens or there is a disruption in signaling (e.g. due to AR mutations), the urethra will end up along the ventral aspect of the shaft or at the base of the clitorophallus. In those who will have a vagina, the urethral plate extends to create part of the vaginal vestibule as well.

The Clitorophallus at the Time of Birth

At the time of birth, the appearance of the clitorophallus plays a key role in the assignment of infant sex and, as a byproduct, gender.[16] Clitorophallus size, association with other genitals (a vagina, testes), and presence of a ventral urethra often guide those who are evaluating a newborn for sex determination. Use of the morphology of the clitorophallus to assign sex, and therefore gender, of child raising originates, in part, within problematic literature suggesting that gender of raising is fully determinative and that therefore children should be provided with the best surgical

outcome[8]. Although gender of raising is highly correlated with adult gender identity, it is far from fully correlated. This can be seen in the existence both endosex transgender populations and intersex individuals who affirm a gender that does not correlate with how they were reared[23,24].

Some researchers have proposed that prenatal androgen exposure affects not just the structures of the clitorophallus but also the brain, and thereby the development of a male or female gender identity. While there is evidence to support this hypothesis, it is difficult to disambiguate the role of non-androgenic effects on identity formation, including both the sex of rearing and the effects of clitorophallus anatomy on self-conceptulatization[9,25,26]. Emerging expert opinion in intersex care recognizes that it is not currently possible to conclusively determine a child's future gender identity at the time of birth, regardless of their hormonal exposure, chromosomal structure, or genital anatomy.[10]

The clitorophallus of a neonate with functional ovaries and no androgenic exposure in utero is typically the smallest, with a separate urethra. The size can vary at time of birth from 3.7mm-7.7mm in length, depending on features of the population studied including race and gestational age.[27–34] The length of a clitorophallus of a patient born with functional testes and AR is typically 3.5cm, with a urethra on the ventral aspect.[35] Micropenis is a term used for a cllitorophallus that is considered > 2.5 standard deviations (SD) smaller than a fully virialized clitorophallus but that still typically has a ventral urethra.[17]

The Prader scale is used to describe the degree of virilization of the clitorophallus at the time of birth and includes evaluation of both size and urethral location[36]. Stage 0 is considered a small clitorophallus, separate urethra (non-virialized). Prader 5 is considered fully virialized. The clitorophallus regardless of size and presence of urethra has the potential for erogenous sensation and orgasmic function.[18]

Neonates who have functional testes typically undergo a minipuberty at around age 3 months. This involves an activation of the hypothalamic, pituitary, gonadal axis, leading to a peak production of testosterone that approaches adult male levels.[37] During this time there can be an enlargement of the clitorophallus. One study has shown that clitorophallus length and growth are both positively correlated with the peak level of testosterone seen in the minipuberty, with an

increase in clitorophallus size occurring from birth to 3 years (from mean 3.5 to 4.5cm) and the maximum velocity from birth to 3 months (one millimeter of growth per month).[38] A study of testosterone replacement therapy in infants has shown that exogenous gonadotropins can stimulate this minipuberty and induce clitorophallus growth (increasing median size from 2cm to 3.8cm), through upregulation of endogenous testosterone production in the testes.[37]

The Clitorophallus at the Time of Puberty

The majority of clitorophallus growth occurs during puberty, which is the next time period of androgen exposure in cisgender, endosex males. In a large study of six thousand cisgender, endosex males, mean penile length prior to age 10 was less than 5cm and increased steadily following the onset of puberty until roughly age 16, with a mean penile length around age 19 of 9 to 10cm.[39] This growth is thought to be predominantly driven by endogenous hormones.

In persons with a small clitorophallus and vulvovaginal tissue, little is known about those structures' androgen receptivity beyond the neonatal period, although there is an abundance of AR present in these tissues.[40] Increasing androgen levels increases the mRNA expression of AR, and mouse models following oophorectomy have decreased AR expression, with increased expression when androgens were provided. In ovariectomized rats, administration of estradiol also decreases AR staining, suggesting there is cross regulation amongst the sex steroids and their receptors.[40] Despite this the clitorophallus does not grow significantly in the pubertal time frame in someone with low androgen exposure. Although there is substantially less data than for the high-androgen population, the average length of the clitorophallus in a low-androgen population has been reported as ranging from .3-1.2cm[41–43].

Using Exogenous Androgens to Modify the Clitorophallus

Clitorophallus Modifications in Patients with Intersex Traits or Differences in Sexual Development

Exogenous testosterone has been used to modify the clitorophallus in both the context of differences of sexual differentiation and gender affirming care. Infants diagnosed with micropenis have been offered short courses of parenteral testosterone enanthate once a month for 3 months to try and increase size.[44] This is typically done around the time of the aforementioned mini puberty. Additional prepubertal treatment is typically avoided to limit the risk of early puberty development or negative effects on final height (through premature closure of the epiphysial plates).

Studies have compared parenteral testosterone to topical testosterone and topical DHT in these cases and found no superiority in any one regimen.[4445] Long term data is lacking in how and if these postnatal regimens impact final penile growth and outcomes are conflicting. One study found that those with a micropenis had greater growth velocity at the time of puberty compared to their peers, but that hormonal therapy didn't ultimately affect length.[46] In those who do receive supplemental androgens prepubertally, it is unclear whether the catch up growth they experience is due to endogenous hormones or the pretreatment.[47–49]

Testosterone has been used prior to hypospadias repair, with the thought that it might improve outcomes by temporarily promoting clitorophallic growth and improved blood supply.[35] The average age of repair typically occurs at 4-18 months of age.[50] A number of studies have looked at presurgical administration of testosterone and found variations in outcomes regarding penile length change (1.01 to 2.7cm) and glans circumference enlargement (2.74 to 3.77cm). [35,51–58] However, others have found no difference in changes in size.[35] Dosing in these approaches also varies, with some papers suggesting a fixed dose vs a weight based dosing schedule. It remains unclear how and whether any measured change influences adult clitorophallus size and whether changes are additive to pubertal androgen exposure or nullified by the changes seen at time of puberty. Most studies have a mean follow up of 7-35 months, which does not allow for observation into puberty.[59]

Clitorophallus Modifications in Gender Affirming Care

To date, no studies have shown that topical or parenteral testosterone on someone with testes and an intact hypothalamic pituitary gonadal axis can definitively affect long-term clitorophallic growth. This may be due to a combination of factors including the maximization of

potential growth during pubertal exposure to high androgens and the saturation of AR in the phallus from endogenous testosterone. In contrast, prior to, or in the absence of, the initiation of gender affirming androgen treatment, transmasculine individuals have clitorophallus that are relatively androgen-naïve. The exceptions are those transmasculine persons with endogenous, hyperandrogenic, intersex variations, such as congenital adrenal hyperplasia, where circulating androgen levels pre and post pubertally may be higher than in someone without those variations. Such individuals may experience, or have experienced, various levels of clitorophallus enlargement due to endogenous hormones.[60]

Gender dysphoric individuals born with a small clitorophallus may desire to enlarge or alter the function of this structure as a part of masculinization therapies.[11] When persons utilize parenteral testosterone for the purposes of gender affirmation, the clitorophallus does enlarge. Enlargement typically occurs within the first years of treatment with maximal growth seen at two years. The clitorophallus volume has been noted to increase four to eight times, and the length can increase as well.[61] Studies have found enlargement of the clitorophallus of up to 3.83-4.6cm over 1-2 years of systemic testosterone treatment.[62,63] It has been suggested that earlier exposure to androgens by patients translates into greater growth. [61] There is presently no data to suggest that androgen levels above cisgender, endosex male ranges lead to additional growth.

There is substantial interest in the question of whether the application of topical testosterone or topical DHT, on top of parenteral testosterone, can lead to additional clitorophallus growth. To date, there have been no studies of topical DHT on clitorophallus size in transmasculine persons. Data as referenced above in cisgender, endosex males has not shown the addition of topical testosterone to parental testosterone to improve clitorophallus growth.[64] However, the hormonal history is different enough in transmasculine persons that a need for formal research is indicated.

Patients may also be interested in using topical testosterone or DHT (not available in the US) to enlarge the clitorophallus when they are not utilizing systemic testosterone with the intended goal of only instituting local changes. While this has not been studied directly in transmasculine persons, topical testosterone has been used in the genitals of persons with lichen sclerosis. While

clitorophallus enlargement has been noted in these studies, they have also found systemic changes seen with testosterone, suggesting that application of topical testosterone to the clitorophallus may still induce systemic effects.[65] Therefore, individuals wishing to avoid the systemic effects of testosterone should be warned that even local application of testosterone may lead to such changes.

Clitorophallus Enlargement and Modification Surgeries

There are limits in the extent of modifications of clitorophallus size and function that can be accomplished using exogenous testosterone. Those individuals who desire structural and functional changes beyond those achievable with hormone therapy may seek out surgical options. Phalloplasty is rarely offered for intersex and endosex men with penile insufficiency, although it is an option[66,67]. In contrast, reconstructive genital surgery for transgender men has gained popularity over the past several decades with social progress, increased visibility & acceptance, and improvements in insurance coverage around the world.

Counseling and Preoperative Considerations

Transmasculine patients who are interested in genital surgery as part of their gender affirmation care have two major options: metoidioplasty and phalloplasty. Phalloplasty involves the use of distant tissue transfer (regional or free-microvascular flap) to create a neophallus to allow the patient the possibility of both voiding in the standing position and participating in sexual penetration[68,69]. Metoidioplasty, in contrast, utilizes the enlarged clitorophallus as the body of the neophallus while adding local tissues to reconstruct into a structure that appears more congruent with expectations of a penis. Metoidioplasty typically includes urethral lengthening so that individuals can urinate while standing, but individuals may not have sufficient length to engage in penetrative intercourse[70]. Certain metoidioplasty techniques require a minimum clitorophallus length prior to surgery, and some surgeons use vacuum stretching and other external protocols to maximize clitorophallus length both prior to and after surgery.[70]

Patient intentions for clitorophallus use are highly variable and need to be assessed individually. The patient should be asked to rate components of their goals and desires such as outward appearance, standing while voiding, sexual penetration, orgasm, and donor site considerations (for phalloplasty). These goals can then be translated into informed decision-making[71]. Patients whose desires fall outside the typical requests should be further vetted and assessed to understand how those desires reflect and interact with their gender identity and psychosocial readiness. Some patients feel best with anatomy that has both penetrative and receptive potential and may request specific sub-procedures. These patients may experience a drive to feel more whole by resolving gender dysphoria, or perhaps feel improved by achieving gender euphoria. The World Professional Association for Transgender Health (WPATH) provides guidelines regarding the assessment and preparation of patients seeking gender affirmation surgery.[72] Regardless of patient goals, adequate clinical and psychosocial preparation for gender affirming surgeries is critical for good outcomes and minimal complications.

Metiodioplasty

The history of Metoidioplasty technique goes back to 1996 where it was first offered as an alternative to phalloplasty[73]. The core purpose of this procedure is to provide patients with the ability to void in the upright position through utilizing modified hypospadias techniques on the enlarged virialized clitorophallus. Typically, metoidioplasty is done in a single stage, but some modifications and revisions may be required later on.

There are several surgical techniques for metoidioplasty, and the majority of surgeons perform vaginectomy, urethral lengthening, and scrotoplasty during this procedure. Incorporating reconstruction of the scrotal sac with placement of testicular implants at the time of the initial surgery allows for a single stage procedure. All metoidioplasty techniques include resection of the suspensory ligaments, which allows the clitorophallus to be stretched and repositioned in a higher position on the pubis symphysis, closer to the position of the cisgender, endosex male clitorophallus (penis) on the pubis symphysis. The major differences between the metoidioplasty techniques are

around the urethral lengthening component and not on the exteriorization and stretching of the enlarged clitorophallus. This portion of the procedure is sometimes described as "clitoral release."[70]

Phalloplasty

The desire to stand to void is the primary reason why people seek metoidioplasty. However, phalloplasty may be desired by patients for a number of reasons**.** Specific goals for phalloplasty may affect technique and flap choice, although the radial forearm free-flap phalloplasty is generally considered to be the gold standard for care[74]. Different surgeons stage their phalloplasty surgeries differently, and there is no clear data on how staging affects outcomes

Reported phalloplasty outcomes are generally satisfactory though most researchers have not assessed long term patient health-related quality of life or satisfaction using validated instruments.[75] High satisfaction and low regret has been reported in a few studies, but most research focuses on complications of these procedures.[76,77] Most reports present high urethral complication rates as the most common problems including strictures, fistulae, and diverticula, and these may require surgical repair.[75,78–80 81]

Sexual Function of the Clitorophallus

The clitorophallus can play an important role in sexual function. Many individuals with a small clitorophallus experience the clitorophallus as a primary site of sexual pleasure, and stimulation of the clitorophallus may be required for some people to achieve orgasm[82,83]. In its native state, the small clitorophallus has erectile function, although it is rare that the length achieved is sufficient for individuals to achieve sexual penetration.

Although sexual penetration is not of interest to all individuals who seek modification of the small clitorophallus, it is important for some.[71,84] Individuals considering metoidioplasty should be advised that they should not anticipate sufficient length after surgery to engage in unassisted penetration, although some metoidioplasty patients do achieve this goal[70]. Some individuals who wish to maintain native erectile function in their clitorophallus, and/or avoid some of the

complications of phalloplasty, may choose to use a strap on or adhered phallic prosthesis to engage in sexual penetration after metoidioplasty, clitoral release, or hormone enlargement.

The neophallus created by phalloplasty does not have native erectile function. Therefore, individuals who wish to engage in sexual penetration with their phallus will need to use a penile prosthesis. Both internal and external prostheses are available, although the only published research is on internal devices.

There are two primary types of internal prostheses, malleable and inflatable. Both inflatable and malleable prostheses have high rates of failure and other complications in transmasculine patients.[85] Reports suggest that a substantial number of devices are removed and/or replaced within the first few years, due to mechanical or other problems. Common non-mechanical complications include infection, migration, and erosion of the device through the neophallus, and a recent systematic review of implants found that complications occurred in 36 percent across all implant types.[86] Failure rates are higher in transgender than cisgender, endosex males in part because these devices were not initially designed for use in the neophallus (Also thought to be related to diminished sensation of the neophallus, which can result in higher risk of trauma/damage). Researchers are also developing prostheses specifically for use after phalloplasty, although it will likely be some time before such devices reach the market.[87]

Conclusion

The clitorophallus can be an important part of an individual's anatomy. It has the highest concentration of nerve endings in the human body, has the ability to become erect, and can contribute to pleasure and orgasm. Much of the development of the clitorophallus is driven by the presence of and response to androgens. Prenatally, this leads to a range of development from the small clitorophallus with external urethra, commonly referred to as the clitoris, to the larger clitorophallus with a ventral urethra, commonly referred to as the penis.

There is mixed evidence about the use of exogenous testosterone to affect the size and function of the clitorophallus. Where people desire changes to their clitorophallus to affirm their gender identity, there are several options. Androgens can be used to enlarge the clitorophallus.

Surgical modifications can be used to change both its size and function, include releasing the fascia, moving the clitorophallus to an anatomic location in line with a penile location, elongating the urethra along the dorsum, and creating a full neophallus. There is less data about the success of using exogenous testosterone on individuals with functional testes, including those with various intersex traits.

Further research is needed to understand the psychological and physical (including urinary and sexual) outcomes of various clitorophallus modifications as well as the reasons people do and do not choose various options. Additional research is also needed to understand which if any post-pubertal hormonal therapies are superior in achieving clitorophallus enlargement in transmasculine individuals with minimal prior androgen exposure.

Authors' Contributions

Frances Grimstad led the literature review curation, led the original draft writing, and participated in the draft review and editing. Elizabeth Boskey supported the literature review curation, supported the original draft writing, and participated in the draft review and editing. Oren Ganor participated in the draft review and editing. Amir Taghinia participated in the draft review and editing. Carlos Estrada participated in the draft review and editing.

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Bibliography

1. Roberts J, Griffiths FE, Verran A, Ayre C. Why do women seek ultrasound scans from commercial providers during pregnancy? *Sociology of Health & Illness*. 2015;37(4):594-609. doi:https://doi.org/10.1111/1467-9566.12218

2. Larkin L. Authentic Mothers, Authentic Daughters and Sons: Ultrasound Imaging and the Construction of Fetal Sex and Gender. *Canadian Review of American Studies*. 2006;36(3):273-292. doi:10.3138/CRAS-s036-03-03

3. Frisch M, Aigrain Y, Barauskas V, et al. Cultural Bias in the AAP's 2012 Technical Report and Policy Statement on Male Circumcision. *Pediatrics*. 2013;131(4):796-800. doi:10.1542/peds.2012-2896

4. Jacobs AJ, Arora KS. Ritual Male Infant Circumcision and Human Rights. *The American Journal of Bioethics*. 2015;15(2):30-39. doi:10.1080/15265161.2014.990162

5. Morris BJ, Moreton S, Krieger JN. Critical evaluation of arguments opposing male circumcision: A systematic review. *Journal of Evidence-Based Medicine*. 2019;12(4):263-290. doi:https://doi.org/10.1111/jebm.12361

6. Karkazis K. *Fixing Sex: Intersex, Medical Authority, and Lived Experience*. Illustrated edition. Duke University Press Books; 2008.

7. Davis G. *Contesting Intersex: The Dubious Diagnosis*. NYU Press; 2015.

8. Fisher AD, Ristori J, Fanni E, Castellini G, Forti G, Maggi M. Gender identity, gender assignment and reassignment in individuals with disorders of sex development: a major of dilemma. *J Endocrinol Invest*. 2016;39(11):1207-1224. doi:10.1007/s40618-016-0482-0

9. Callens N, Van Kuyk M, van Kuppenveld JH, et al. Recalled and current gender role behavior, gender identity and sexual orientation in adults with Disorders/Differences of Sex Development. *Horm Behav*. 2016;86:8-20. doi:10.1016/j.yhbeh.2016.08.008

10. Krege S, Eckoldt F, Richter-Unruh A, et al. Variations of sex development: The first German interdisciplinary consensus paper. *J Pediatr Urol*. 2019;15(2):114-123. doi:10.1016/j.jpurol.2018.10.008

11. James SE, Herman JL, Keisling M, Mottet L, Anafi M. *The Report of the 2015 US Transgender Survey*. National Center for Transgender Equality; 2016.

12. Cohn MJ. Development of the external genitalia: conserved and divergent mechanisms of appendage patterning. *Dev Dyn*. 2011;240(5):1108-1115. doi:10.1002/dvdy.22631

13. Cunha GR, Liu G, Sinclair A, et al. Androgen-independent events in penile development in humans and animals. *Differentiation*. 2020;111:98-114. doi:10.1016/j.diff.2019.07.005

14. Baskin L, Shen J, Sinclair A, et al. Development of the human penis and clitoris. *Differentiation*. 2018;103:74-85. doi:10.1016/j.diff.2018.08.001

15. Baskin L, Cao M, Sinclair A, et al. Androgen and estrogen receptor expression in the developing human penis and clitoris. *Differentiation*. 2020;111:41-59. doi:10.1016/j.diff.2019.08.005

16. Lee PA, Houk CP, Ahmed SF, Hughes IA. Consensus Statement on Management of Intersex Disorders. *Pediatrics*. 2006;118(2):e488-e500. doi:10.1542/peds.2006-0738

17. Zheng Z, Armfield BA, Cohn MJ. Timing of androgen receptor disruption and estrogen exposure underlies a spectrum of congenital penile anomalies. *Proc Natl Acad Sci U S A*. 2015;112(52):E7194-7203. doi:10.1073/pnas.1515981112

18. Makiyan Z. Systematization of ambiguous genitalia. *Organogenesis*. 2016;12(4):169-182. doi:10.1080/15476278.2016.1210749

19. Savchuk I, Morvan ML, Antignac JP, et al. The human genital tubercle is steroidogenic organ at early pregnancy. *Molecular and Cellular Endocrinology*. 2018;477:148-155. doi:10.1016/j.mce.2018.06.012

20. O'Shaughnessy PJ, Antignac JP, Le Bizec B, et al. Alternative (backdoor) androgen production and masculinization in the human fetus. *PLoS Biol*. 2019;17(2):e3000002. doi:10.1371/journal.pbio.3000002

21. Kaňová N, Bičíková M. Hyperandrogenic states in pregnancy. *Physiol Res*. 2011;60(2):243-252. doi:10.33549/physiolres.932078

22. Morris LF, Park S, Daskivich T, et al. Virilization of a female infant by a maternal adrenocortical carcinoma. *Endocr Pract*. 2011;17(2):e26-31. doi:10.4158/EP10209.CR

23. Babu R, Shah U. Gender identity disorder (GID) in adolescents and adults with differences of sex development (DSD): A systematic review and meta-analysis. *J Pediatr Urol*. Published online November 12, 2020. doi:10.1016/j.jpurol.2020.11.017

24. Herman JL, Flores AR, Brown TNT, Wilson BDM, Conron KJ. *Age of Individuals Who Identify as Transgender in the United States*. The Williams Institute; 2017:13. https://williamsinstitute.law.ucla.edu/wp-content/uploads/TransAgeReport.pdf

25. Nguyen HB, Loughead J, Lipner E, Hantsoo L, Kornfield SL, Epperson CN. What has sex got to do with it? The role of hormones in the transgender brain. *Neuropsychopharmacology*. 2019;44(1):22-37. doi:10.1038/s41386-018-0140-7

26. Joseph AA, Kulshreshtha B, Mehta M, Ammini AC. Sex of rearing seems to exert a powerful influence on gender identity in the absence of strong hormonal influence: report of two siblings with PAIS assigned different sex of rearing. *J Pediatr Endocrinol Metab*. 2011;24(11-12):1071-1075. doi:10.1515/jpem.2011.287

27. Phillip M, De Boer C, Pilpel D, Karplus M, Sofer S. Clitoral and penile sizes of full term newborns in two different ethnic groups. *J Pediatr Endocrinol Metab*. 1996;9(2):175-179.

28. Oberfield SE, Mondok A, Shahrivar F, Klein JF, Levine LS. Clitoral size in full-term infants. *Am J Perinatol*. 1989;6(4):453-454. doi:10.1055/s-2007-999638

29. Niklasson A, Albertsson-Wikland K. Continuous growth reference from 24th week of gestation to 24 months by gender. *BMC Pediatr*. 2008;8:8. doi:10.1186/1471-2431-8-8

30. KUTLU H, Akbiyik F. Clitoral length in female newborns: A new approach to the assessment of clitoromegaly. *Turkish Journal of Medical Sciences*. 2011;41:495-499. doi:10.3906/sag-1006-907

31. Won SY, Koh MW, Lee TH, Eun MJ, Kim JS, Kim OK. The Clitoral Size of the Korean Female Newborn. *Yeungnam University Journal of Medicine*. 2001;18(2):287-292. doi:2001.18.2.287

32. Alaei M, Rohani F, Norouzi E, et al. The Nomogram of Clitoral Length and Width in Iranian Term and Preterm Neonates. *Front Endocrinol*. 2020;11. doi:10.3389/fendo.2020.00297

33. Castets S, Nguyen K-A, Plaisant F, et al. Reference values for the external genitalia of full-term and pre-term female neonates. *Archives of Disease in Childhood - Fetal and Neonatal Edition*. 2021;106(1):39-44. doi:10.1136/archdischild-2019-318090

34. Asafo-Agyei SB, Ameyaw E, Chanoine J-P, Zacharin M, Nguah SB. Clitoral size in term newborns in Kumasi, Ghana. *Int J Pediatr Endocrinol*. 2017;2017:6. doi:10.1186/s13633-017-0045-y

35. Kaya C, Radmayr C. The role of pre-operative androgen stimulation in hypospadias surgery. *Transl Androl Urol*. 2014;3(4):340-346. doi:10.3978/j.issn.2223-4683.2014.12.01

36. Prader A. [Genital findings in the female pseudo-hermaphroditism of the congenital adrenogenital syndrome; morphology, frequency, development and heredity of the different genital forms]. *Helv Paediatr Acta*. 1954;9(3):231-248.

37. Papadimitriou DT, Chrysis D, Nyktari G, et al. Replacement of Male Mini-Puberty. *Journal of the Endocrine Society*. 2019;3(7):1275-1282. doi:10.1210/js.2019-00083

38. Boas M, Boisen KA, Virtanen HE, et al. Postnatal penile length and growth rate correlate to serum testosterone levels: a longitudinal study of 1962 normal boys. *Eur J Endocrinol*. 2006;154(1):125-129. doi:10.1530/eje.1.02066

39. Tomova A, Deepinder F, Robeva R, Lalabonova H, Kumanov P, Agarwal A. Growth and development of male external genitalia: a cross-sectional study of 6200 males aged 0 to 19 years. *Arch Pediatr Adolesc Med*. 2010;164(12):1152-1157. doi:10.1001/archpediatrics.2010.223

40. Palacios S. Expression of androgen receptors in the structures of vulvovaginal tissue. *Menopause*. 2020;27(11):1336-1342. doi:10.1097/GME.0000000000001587

41. Ellibeş Kaya A, Doğan O, Yassa M, Başbuğ A, Özcan C, Çalışkan E. Do external female genital measurements affect genital perception and sexual function and orgasm? *Turk J Obstet Gynecol*. 2020;17(3):175-181. doi:10.4274/tjod.galenos.2020.89896

42. Jackson LA, Hare AM, Carrick KS, Ramirez DMO, Hamner JJ, Corton MM. Anatomy, histology, and nerve density of clitoris and associated structures: clinical applications to vulvar surgery. *Am J Obstet Gynecol*. 2019;221(5):519.e1-519.e9. doi:10.1016/j.ajog.2019.06.048

43. Verkauf BS, Von Thron J, O'Brien WF. Clitoral size in normal women. *Obstet Gynecol*. 1992;80(1):41-44.

44. Wiygul J, Palmer LS. Micropenis. *ScientificWorldJournal*. 2011;11:1462-1469. doi:10.1100/tsw.2011.135

45. Sasaki G, Ishii T, Hori N, et al. Effects of pre- and post-pubertal dihydrotestosterone treatment on penile length in 5α-reductase type 2 deficiency. *Endocr J*. 2019;66(9):837-842. doi:10.1507/endocrj.EJ19-0111

46. Han JH, Lee JP, Lee JS, Song SH, Kim KS. Fate of the micropenis and constitutional small penis: do they grow to normalcy in puberty? *Journal of Pediatric Urology*. 2019;15(5):526.e1-526.e6. doi:10.1016/j.jpurol.2019.07.009

47. Ishii T, Sasaki G, Hasegawa T, Sato S, Matsuo N, Ogata T. Testosterone enanthate therapy is effective and independent of SRD5A2 and AR gene polymorphisms in boys with micropenis. *J Urol*. 2004;172(1):319-324. doi:10.1097/01.ju.0000129005.84831.1e

48. Bin-Abbas B, Conte FA, Grumbach MM, Kaplan SL. Congenital hypogonadotropic hypogonadism and micropenis: effect of testosterone treatment on adult penile size why sex reversal is not indicated. *J Pediatr*. 1999;134(5):579-583. doi:10.1016/s0022-3476(99)70244-1

49. Klugo RC, Cerny JC. Response of micropenis to topical testosterone and gonadotropin. *J Urol*. 1978;119(5):667-668. doi:10.1016/s0022-5347(17)57584-9

50. Mohammadipour A, Hiradfar M, Sharifabad PS, Shojaeian R. Pre-operative hormone stimulation in hypospadias repair: A facilitator or a confounder. *J Pediatr Urol*. 2020;16(3):318.e1-318.e7. doi:10.1016/j.jpurol.2020.04.012

51. Ishii T, Hayashi M, Suwanai A, Amano N, Hasegawa T. The effect of intramuscular testosterone enanthate treatment on stretched penile length in prepubertal boys with hypospadias. *Urology*. 2010;76(1):97-100. doi:10.1016/j.urology.2009.12.065

52. Nerli RB, Koura A, Prabha V, Reddy M. Comparison of topical versus parenteral testosterone in children with microphallic hypospadias. *Pediatr Surg Int*. 2009;25(1):57-59. doi:10.1007/s00383-008-2278-6

53. Luo CC, Lin JN, Chiu CH, Lo FS. Use of parenteral testosterone prior to hypospadias surgery. *Pediatr Surg Int*. 2003;19(1-2):82-84. doi:10.1007/s00383-002-0717-3

54. Chalapathi G, Rao KLN, Chowdhary SK, Narasimhan KL, Samujh R, Mahajan JK. Testosterone therapy in microphallic hypospadias: Topical or parenteral? *Journal of Pediatric Surgery*. 2003;38(2):221-223. doi:10.1053/jpsu.2003.50047

55. Davits RJ a. M, Aker ESSV den, Scholtmeijer RJ, Keizer-Schrama SMPFDM, Nijman RJM. Effect of Parenteral Testosterone Therapy on Penile Development in Boys with Hypospadias. *British Journal of Urology*. 1993;71(5):593-595. doi:https://doi.org/10.1111/j.1464-410X.1993.tb16031.x

56. Gearhart JP, Jeffs RD. The use of parenteral testosterone therapy in genital reconstructive surgery. *J Urol*. 1987;138(4 Pt 2):1077-1078. doi:10.1016/s0022-5347(17)43507-5

57. Tsur H, Shafir R, Shachar J, Eshkol A. Microphallic hypospadias: testosterone therapy prior to surgical repair. *Br J Plast Surg*. 1983;36(3):398-400. doi:10.1016/s0007-1226(83)90069-3

58. Monfort G, Lucas C. Dehydrotestosterone penile stimulation in hypospadias surgery. *Eur Urol*. 1982;8(4):201-203. doi:10.1159/000473517

59. Wong NC, Braga LH. The Influence of Pre-Operative Hormonal Stimulation on Hypospadias Repair. *Front Pediatr*. 2015;3. doi:10.3389/fped.2015.00031

60. Iezzi ML, Lasorella S, Varriale G, Zagaroli L, Ambrosi M, Verrotti A. Clitoromegaly in Childhood and Adolescence: Behind One Clinical Sign, a Clinical Sea. *SXD*. 2018;12(4):163-174. doi:10.1159/000489385

61. Gooren LJG, Giltay EJ. Review of Studies of Androgen Treatment of Female-to-Male Transsexuals: Effects and Risks of Administration of Androgens to Females. *The Journal of Sexual Medicine*. 2008;5(4):765-776. doi:10.1111/j.1743-6109.2007.00646.x

62. Fisher AD, Castellini G, Ristori J, et al. Cross-Sex Hormone Treatment and Psychobiological Changes in Transsexual Persons: Two-Year Follow-Up Data. *J Clin Endocrinol Metab*. 2016;101(11):4260-4269. doi:10.1210/jc.2016-1276

63. Meyer WJ, Webb A, Stuart CA, Finkelstein JW, Lawrence B, Walker PA. Physical and hormonal evaluation of transsexual patients: A longitudinal study. *Arch Sex Behav*. 1986;15(2):121-138. doi:10.1007/BF01542220

64. Krishnan A, Chagani S, Rohl AJ. Preoperative Testosterone Therapy Prior to Surgical Correction of Hypospadias: A Review of the Literature. *Cureus*. 8(7). doi:10.7759/cureus.677

65. Chi C, Kirtschig G, Baldo M, Brackenbury F, Lewis F, Wojnarowska F. Topical interventions for genital lichen sclerosus. *Cochrane Database Syst Rev*. 2011;2011(12). doi:10.1002/14651858.CD008240.pub2

66. Callens N, De Cuypere G, Van Hoecke E, et al. Sexual quality of life after hormonal and surgical treatment, including phalloplasty, in men with micropenis: a review. *J Sex Med*. 2013;10(12):2890-2903. doi:10.1111/jsm.12298

67. Falcone M, Garaffa G, Raheem A, Christopher NA, Ralph DJ. Total Phallic Reconstruction Using the Radial Artery Based Forearm Free Flap After Traumatic Penile Amputation. *J Sex Med*. 2016;13(7):1119-1124. doi:10.1016/j.jsxm.2016.05.003

68. Frey JD, Poudrier G, Chiodo MV, Hazen A. A Systematic Review of Metoidioplasty and Radial Forearm Flap Phalloplasty in Female-to-male Transgender Genital Reconstruction: Is the "Ideal" Neophallus an Achievable Goal? *Plast Reconstr Surg Glob Open*. 2016;4(12):e1131. doi:10.1097/GOX.0000000000001131

69. Morrison SD, Shakir A, Vyas KS, Kirby J, Crane CN, Lee GK. Phalloplasty: A Review of Techniques and Outcomes. *Plastic and Reconstructive Surgery*. 2016;138(3):594-615. doi:10.1097/PRS.0000000000002518

70. Jolly D, Wu CA, Boskey ER, Taghinia AH, Diamond DA, Ganor O. Is Clitoral Release Another Term for Metoidioplasty? A Systematic Review and Meta-Analysis of Metoidioplasty Surgical Technique and Outcomes. *Sexual Medicine*. 2021;9(1):100294. doi:10.1016/j.esxm.2020.100294

71. Ganor O, Taghinia AH, Diamond DA, Boskey ER. Piloting a Genital Affirmation Surgical Priorities Scale for Trans Masculine Patients. *Transgend Health*. 2019;4(1):270-276. doi:10.1089/trgh.2019.0038

72. Coleman E, Bockting W, Botzer M, et al. Standards of Care for the Health of Transsexual, Transgender, and Gender-Nonconforming People, Version 7. *International Journal of Transgenderism*. 2012;13(4):165-232. doi:10.1080/15532739.2011.700873

73. Hage JJ. Metaidoioplasty: An Alternative Phalloplasty Technique in Transsexuals. *Plastic and Reconstructive Surgery*. 1996;97(1):161.

74. Yao A, Ingargiola MJ, Lopez CD, et al. Total penile reconstruction: A systematic review. *J Plast Reconstr Aesthet Surg*. 2018;71(6):788-806. doi:10.1016/j.bjps.2018.02.002

75. Morrison SD, Shakir A, Vyas KS, Kirby J, Crane CN, Lee GK. Phalloplasty: A Review of Techniques and Outcomes. *Plast Reconstr Surg*. 2016;138(3):594-615. doi:10.1097/PRS.0000000000002518

76. Garcia MM, Christopher NA, De Luca F, Spilotros M, Ralph DJ. Overall satisfaction, sexual function, and the durability of neophallus dimensions following staged female to male genital gender confirming surgery: the Institute of Urology, London U.K. experience. *Transl Androl Urol*. 2014;3(2):156-162. doi:10.3978/j.issn.2223-4683.2014.04.10

77. Wierckx K, Van Caenegem E, Elaut E, et al. Quality of life and sexual health after sex reassignment surgery in transsexual men. *J Sex Med*. 2011;8(12):3379-3388. doi:10.1111/j.1743-6109.2011.02348.x

78. Ascha M, Massie JP, Morrison SD, Crane CN, Chen ML. Outcomes of Single Stage Phalloplasty by Pedicled Anterolateral Thigh Flap versus Radial Forearm Free Flap in Gender Confirming Surgery. *J Urol*. 2018;199(1):206-214. doi:10.1016/j.juro.2017.07.084

79. Jun MS, Santucci RA. Urethral stricture after phalloplasty. *Transl Androl Urol*. 2019;8(3):266-272. doi:10.21037/tau.2019.05.08

80. Heston AL, Esmonde NO, Dugi DD, Berli JU. Phalloplasty: techniques and outcomes. *Transl Androl Urol*. 2019;8(3):254-265. doi:10.21037/tau.2019.05.05

81. Santucci RA. Urethral Complications After Transgender Phalloplasty: Strategies to Treat Them and Minimize Their Occurrence. *Clin Anat*. 2018;31(2):187-190. doi:10.1002/ca.23021

82. Shirazi T, Renfro KJ, Lloyd E, Wallen K. Women's Experience of Orgasm During Intercourse: Question Semantics Affect Women's Reports and Men's Estimates of Orgasm Occurrence. *Arch Sex Behav*. 2018;47(3):605-613. doi:10.1007/s10508-017-1102-6

83. Herbenick D, Fu T-CJ, Arter J, Sanders SA, Dodge B. Women's Experiences With Genital Touching, Sexual Pleasure, and Orgasm: Results From a U.S. Probability Sample of Women Ages 18 to 94. *J Sex Marital Ther*. 2018;44(2):201-212. doi:10.1080/0092623X.2017.1346530

84. van de Grift TC, Pigot GLS, Boudhan S, et al. A Longitudinal Study of Motivations Before and Psychosexual Outcomes After Genital Gender-Confirming Surgery in Transmen. *J Sex Med*. 2017;14(12):1621-1628. doi:10.1016/j.jsxm.2017.10.064

85. van der Sluis WB, Pigot GLS, Al-Tamimi M, et al. A Retrospective Cohort Study on Surgical Outcomes of Penile Prosthesis Implantation Surgery in Transgender Men After Phalloplasty. *Urology*. 2019;132:195-201. doi:10.1016/j.urology.2019.06.010

86. Rooker SA, Vyas KS, DiFilippo EC, Nolan IT, Morrison SD, Santucci RA. The Rise of the Neophallus: A Systematic Review of Penile Prosthetic Outcomes and Complications in Gender-

Affirming Surgery. *The Journal of Sexual Medicine*. 2019;16(5):661-672. doi:10.1016/j.jsxm.2019.03.009

87. Neuville P, Morel-Journel N, Cabelguenne D, Ruffion A, Paparel P, Terrier J-E. First Outcomes of the ZSI 475 FtM, a Specific Prosthesis Designed for Phalloplasty. *J Sex Med*. 2019;16(2):316-322. doi:10.1016/j.jsxm.2018.11.013

Table 1: Definitions

Term	Definition
Clitorophallus	A unifying term used to describe the postnatal structure which develops from the genital tubercle in utero. This structure may grow in response to androgens pre- or post-natal and may also have a urethra along the ventral aspect. It is typically referred to as the clitoris in endosex females and the penis in endosex males.
Clitoris	The term typically used when the clitorophallus is small, without long corpus cavernosa and without a urethra on the ventral aspect (as in many endosex females).
Penis	The term typically used when the clitorophallus is larger (10cm), with long corpus cavernosa and with a urethra along the ventral aspect which emerges at the glans (as in many endosex males)
Intersex	Someone whose genitalia, hormones, internal reproductive anatomy, or chromosomes, do not align with what is expected of the male-female sex binary.
Endosex	Someone whose genitalia, hormones, internal reproductive anatomy and chromosomes align with what is expected of the male-female sex binary
Transgender	Someone whose gender identity does not align with what is expected of their assigned sex at birth.
Cisgender	Someone whose gender identity aligns with what is expected of their assigned sex at birth.