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Review

Dermatologic care of the transgender patient

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ABSTRACT

Literature is limited regarding the medical and cosmetic dermatologic issues pertinent to transgender patients and the reasons why transgender individuals seek care from dermatologists. Clinical management of this population has historically been limited to mental health providers, endocrinologists, and select surgeons with expertise in sex reassignment surgery. The impact of hormonal therapy on transgender skin has been well documented in endocrinology journals, but is underrepresented in dermatology literature. Hormonal therapy leads to drastic skin alterations, impacting sebum production, hair growth, and acne, all of which may become a dermatologic concern for the transgender patient. Dermatologists may also be consulted regarding issues such as permanent hair removal, androgenic alopecia, or scar revision following breast reduction surgery or genital reassignment surgery. The purpose of this review is to provide relevant information for use by all dermatology providers who care for transgender patients or patients undergoing transition.

INTRODUCTION

Transsexualism is a condition characterized by gender dysphoria, which, according to the Diagnostic and Statistical Manual, 5th Edition, is defined as an incongruence between a person's gender identity (i.e. their experienced or expressed gender) and his or her somatic gender for at least 6 months duration. It is often accompanied by the desire to live as the opposite gender hormonally, anatomically, and psychologically. Transsexualism is expressed in many different ways, one form being the alteration of somatic gender through hormonal and surgical treatment [1-3]. The term transsexual refers to those committed to transforming their bodies into that of their identified gender, whereas "transgender" is a generic term used to describe those whose gender identity differs from their biological sex [4].

In the Netherlands, the prevalence of transsexualism is 1 in 11,900 genotypic men and 1 in 30,400 genotypic women [5]. Determining the prevalence of transsexualism in the United States is limited by lack of case registries. In recent years, an increasing number of people in the United States have come forward as transgender, and at younger ages [4]. Greater openness to and acceptance of gender variance, along with heightened media portrayal of transgender individuals, have increased awareness of this population's specific healthcare needs.

An article by Katz et al [6] describing the dermatology-related, epidemiologic concerns of sexual minorities established that transgender individuals possess a unique set of skin-related challenges that may motivate them to present to a dermatologist. These challenges include managing the skin-related changes accompanying cross-sex hormone therapy and/or sex change surgery, addressing the increased prevalence of HIV in this population (resulting in HIV-related dermatologic manifestations), and uncovering the health risks associated with “pumping parties.” Pumping parties refer to an underground industry targeted toward the transgender community (particularly male-to-female [MTF] transsexuals), in which anonymous, unlicensed individuals supply and inject non-medical grade “silicone” into the hips and buttocks of patients seeking a more feminine shape [7]. Only 4 reports in the medical literature have discussed pumping parties, thus highlighting a knowledge gap for dermatology providers.

Transsexual patients desiring the fullest possible transformation into the opposite gender need medical evaluation and treatment by healthcare practitioners. Treatments involved in the transition process lead to multiple skin changes, and sometimes dermatologic disease, making this topic relevant for providers. This article provides a review of the common dermatologic sequelae associated with transsexual individuals undergoing sex change, along with other dermatologic concerns that specifically affect the transgender population.

HORMONAL EFFECTS ON SKIN AND HAIR

Prior to commencing any form of treatment, the diagnoses of gender dysphoria and transsexualism must first be established by a mental health professional. Individuals treated with cross-sex hormones are considered eligible for sex reassignment surgery after having successfully lived as their desired gender for at least 12 months, and after having continuously used cross-sex hormones responsibly for one year or longer [8]. Because cross-sex hormone therapy precedes sex-reassignment surgery by at least a year, dermatologic changes are likely to occur at this stage of transition.

Hormonal reassignment achieves two aims: (1) to reduce the hormonally-mediated, secondary sex characteristics of the original sex, and (2) to acquire the secondary sex characteristics of the new sex to the fullest extent possible [9].

Skin

Sex hormones, particularly androgens, regulate sebaceous gland and hair growth by activating epithelial sebocytes and the dermal papilla of the hair follicle [10]. The skin is a minor source of androgen synthesis in the body. Dehydroepiandrosterone sulfate (DHEA-S) and androstenedione are circulating androgens produced in the adrenal gland of both genders. These androgens reach the skin through the bloodstream, and are converted into the more potent androgens, testosterone and dihydrotestosterone (DHT), by enzymes found in sebocytes, sweat glands, and dermal papilla cells [11]. Sebocytes produce and secrete lipid-rich sebum into the hair canal and onto the skin surface [12-14]. Normally functioning sebaceous glands are integral to skin homeostasis and barrier control [12]. Through intracrine and paracrine mechanisms, androgens also mediate hair growth, hair follicle size, perspiration, and in susceptible men, alopecia [11].

The disruption of these normal regulatory pathways by antiandrogenic medications used by MTF individuals may lead to xerosis and nail fragility [9], whereas other patients report skin softening. Reduced sebaceous gland activity secondary to antiandrogen therapy also minimizes acne owing to lowered sebum production.

Male-to-female transgender skin:

For MTF transsexuals, administration of estrogens coupled with an androgen suppression agent is considered standard therapy and is more effective than estrogen alone in achieving female phenotype. Additionally, combination therapy allows for lower doses of estrogen to be administered. Oral 17-beta-estradiol valerate (2-4 mg/day) or transdermal 17-beta-estradiol (100 micrograms twice a week) are commonly used formulations. These are less thrombogenic than the previously used oral ethinyl estradiol. Examples of androgen-suppressing agents include cyproterone acetate (commonly used in Europe), medroxyprogesterone acetate, non-steroidal antiandrogens such as flutamide and nilutamide, spironolactone, or 5-alpha-reductase inhibitors such as finasteride [9].

In a study of 21 MTF transsexuals receiving combined estrogen/antiandrogens, a sharp decrease in measurable sebum production (measured by clinicians using Sebutape) occurred at four months after initiation of therapy, and remained lower than pre-treatment

values throughout the one-year duration of the study [15]. An improvement in existing acne may result from hormonal therapy for MTF transsexual patients.

Research has been published to suggest that hormone replacement therapy may increase the risk of developing melanoma. A population based, case-control study by Koomen et al reveals increased risk of developing cutaneous melanoma in association with hormone replacement therapy (HRT) with an odds ratio of 2.08 in women (non-transgender) who had used HRT for 6 months or longer (95% CI 1.37-3.14) [16]. This further underscores the need for performing full-body exams regularly in MTF transgender women taking HRT. In Koomen's study, the more common formulations of HRT included: ethinylestradiol (83.4%), estradiol (9.1%), and conjugated estrogen (4.8%) [16]. There remains conflicting evidence regarding the increased risk of developing non-melanoma skin cancers in association with hormone replacement therapy. Data derived from the "Diet, Cancer and Health Study" demonstrated an increased incidence ratio of 1.15 of basal cell carcinoma in women who had used HRT compared to women who never used it, irrespective of duration. There was an increased risk of developing squamous cell carcinoma (incidence rate ratio 1.35) associated with prolonged use of HRT (greater than 5 years) [17]. Other studies have not observed this association. Post hoc analyses of the Women's Health Initiative randomized placebo-controlled hormone therapy trials showed that rates of nonmelanoma skin cancer and melanoma were similar between the active hormone group (combined analysis of Estrogen + Progesterone and E-alone) and the placebo group [18].

Female-to-male transgender skin:

Female-to-male (FTM) transsexuals employ testosterone treatment to achieve virilization. Intramuscularly administered testosterone esters are most commonly used. Goals of treatment include achieving male vocal pitch, male pattern of sexual hair growth, and stopping menses. Formulations include testosterone ester preparations (testosterone enanthate or cypionate) administered intramuscularly in doses of 100 mg to 200 mg every two weeks. In Europe, testosterone undecanoate 1000 mg intramuscular injections can be given every 12 weeks [4, 8].

Owing to androgenic stimulation of the pilosebaceous unit, acne develops in approximately 40% of subjects [9]. Androgens stimulate sebum production and cause a modest increase in skin temperature [15]. A prospective study of FTM transsexuals initiating hormone therapy with testosterone undecanoate revealed the presence of facial acne in 82% of participants after six months of therapy (35% of participants had facial acne prior to initiation). Back/chest acne increased drastically to 88% of study participants (from 15% prior to hormone use) after six months. The majority of subjects rated their acne as mild or moderate; none had considered their acne to be severe. Approximately 50% of participants used one or more topical acne products within the first year of testosterone administration [19]. Elevated androgens in general have been associated with acne, even in non-transgender women, as evidenced by acne's increased prevalence in women with hyperandrogenemia. Trials evaluating whether acne induced by testosterone injections is responsive to conventional treatment are lacking in the FTM transgender population.

Even in biological, non-transgender women, androgens have been shown to contribute to the development of acne through the same pathophysiologic mechanisms as described above. Both endogenous and exogenous increases in androgens are associated with the development of acne. Common causes of elevated endogenous androgens include polycystic ovarian syndrome, and more uncommonly, adrenal hyperplasia, ovarian hyperthecosis, or virilizing tumors [20]. Biologic women have been shown to develop acne from administration of anabolic steroids or from the use of progestin-only contraceptives containing pro-androgenic progestins [21]. The use of testosterone supplementation in biologic men (for the treatment of hypogonadism) is associated with acne. A prior case report described the development of acne fulminans in a male body builder, induced by anabolic steroids [22].

There are no current guidelines in the treatment of acne in FTM transsexuals, and further studies are needed to determine optimal treatment strategies. Hormonal treatments traditionally used for hyperandrogen states in women (such as PCOS), including oral contraceptive pills, spironolactone, or flutamide, contradict the desired effect of masculinization in MTF patients receiving testosterone and are not recommended in this population. Therefore, it is reasonable to approach the treatment of acne similar to that of non-transgender patients, starting with topical retinoids for mild comedonal acne, with consideration of adding either topical or oral antibiotics for moderate papulopustular or nodular acne [23-24]. Oral isotretinoin has been shown in case reports to be an effective treatment for acne in two FTM transgender individuals on chronic testosterone; one patient received 20mg/daily for 8 months, and the other received 30mg/daily for 9 months. Both had complete resolution of acne [25]. As testosterone is often a permanent therapy for trans men, long-term acne treatment may be necessary.

Hair

Estrogens coupled with antiandrogens reduce hair growth of the legs, cheek, and upper abdomen. MTF transsexuals receiving combined estrogen/antiandrogen therapy exhibit a sharp fall in hair shaft diameter (thickness) within approximately 4 months [15]. Following this, further hair diameter reductions are minimal. In contrast, hair length (as measured by growth rate) decreases slowly and progressively over time; this observation suggests that hair length and hair width may be influenced by different regulatory pathways [15].

The resistance of beard growth (relative to other hair locations) to androgen suppression has been described anecdotally. This may be related to higher hair density and hair shaft diameters on the face. For this reason, MTF transsexuals often seek additional measures to eliminate facial hair, including electrolysis or laser treatment [4]. There have been no studies comparing the efficacy of different hair removal methods in this population, or whether additional treatments are necessary. Nevertheless, the elimination of facial hair remains a leading concern and source of anxiety for many MTF transgender patients. There have also been no studies investigating whether hair removal procedures are more or less effective if done before or after hormonal therapy is started. Anecdotally, most MTF transgender women consider hair removal during the early part of the transition process, though cost and access to a hair removal expert may result in delays.

In the transgender community, electrolysis is frequently sought after as desirable option for hair removal, given its ability to permanently remove facial hair. Although this technique is usually not performed by dermatologists, dermatologists should possess basic knowledge of the procedure in order to assist with in-depth discussions regarding different options for hair removal. Electrolysis involves the insertion of a fine needle into the hair follicle and applying an electric current to destroy the rapidly dividing cells of the matrix and the hair follicle itself. This is often done in a spa-like setting and there are variable results depending on the experience of the proceduralist. In the most experienced hands, many patients undergo permanent hair destruction, with only 15-25% hair regrowth after 6 months [26]. Notable side effects dermatologists must be aware of include erythema, postinflammatory pigment changes, scarring, and flare of herpes simplex virus infection (in patients with prior history of herpes).

Photoepilation therapies (laser and intense pulsed noncoherent light) are additional methods for hair removal through selective photothermolysis. Total removal of hair is uncommon with photoepilation; therefore, realistic expectations with treatment include less hair, lighter hair, and thinner hair. In general, dark hair responds best. The lack of permanency makes this method anecdotally less desired by MTF transgender patients, though it may be an acceptable alternative for some. Patients typically require four to six treatments spaced approximately four to six weeks apart in order to achieve satisfactory hair removal [27].

Eflornithine cream is FDA approved for removal of facial hair in women. As with other forms of hair removal, no studies have been done on transgender individuals. Hair growth is reduced by the irreversible inhibition of ornithine decarboxylase, a key enzyme involved in hair growth. Noticeable results take about six to eight weeks, though once the cream is stopped, hair returns to pretreatment levels after approximately two months. The lack of permanence may make this option less ideal for trans women. Dermatologists should be aware of the relatively high rate of acneiform reactions associated with eflornithine in 10-20% of patients [28].

Conversely, hair growth is the desired outcome for FTM transsexuals undergoing testosterone therapy. Weirckx and colleagues [19] demonstrated that for 20 FTM transsexuals initiating testosterone undecanoate every three months, 100% of subjects eventually experienced increased facial and body hair growth. After six months of treatment, more than half the study population had subjective Ferriman and Gallwey scores of 8 or higher, denoting clinical hirsutism. After 12 months of treatment, 80% of study participants had scores of 8 or higher [19]. However, after 12 months of testosterone therapy, hair diameter did not achieve similar thickness to that of biologic men. Thus, exposure to testosterone therapy of greater than one year may be needed to achieve the same hair diameter as biologic men [15].

The prevalence of androgenic alopecia increases with longer exposure to testosterone. A cross sectional study of 50 FTM transsexuals receiving hormonal therapy for an average of 10 years revealed 31% having moderate to severe alopecia [19]. A significant correlation between alopecia and age was observed. No significant correlation was noted between duration of testosterone therapy, type of testosterone therapy (intramuscular, intramuscular depot, or transdermal) and alopecia [19]. Studies

are lacking regarding optimal treatment for androgenic alopecia associated with testosterone injection, and little data exists regarding efficacy of drugs such as finasteride, dutasteride, or topical minoxidil in this population.

Silicone Injections and pumping parties

The prevalence of illicit silicone or filler use in the transsexual population has been variably reported with estimates ranging from 16.7% in a 2013 population-based sample of trans women in San Francisco, to 29% reported in a 2006 sample of transsexual youth in Chicago [29]. These procedures, often administered on breast, hips, and buttock regions, may be sought after by MTF transsexuals to achieve a more feminized appearance. Serious medical and dermatologic complications may arise due to incorrect placement, large-volume injections, migration, use of adulterated or non-medical grade products, or a combination of the above. The dermatologist or plastic surgeon plays a critical role in recognizing and addressing these complications [30].

In the United States, injected silicone is FDA approved only for intraocular injections in the treatment of retinal detachment. It has not been approved by the FDA for soft tissue augmentation, although it is currently used off-label by some practitioners for this purpose. The exact potential for long-term complications is unknown owing to a lack of randomized-control trials evaluating its use.

Silicone injections are used to fill in sunken tissues either directly with the material, or via collagen formation stimulated around each silicone microdroplet. [31-32]. The microdroplet serial puncture technique has been suggested to minimize complications. This involves subdermal injections of 0.01 mL or less at 2-10 mm apart with a 27-30 gauge needle. In general, 0.5-1 mL total volume is the limit per treatment session. Sessions should be separated by at least 1 month to provide optimal recovery time and collagen formation. Optimal collagen formation usually occurs after 12 weeks [31].

As the majority of desired cosmetic procedures are not covered by insurance benefits, many MTF transgender patients obtain illicit filler injections to obtain their desired body contours at a fraction of the cost. In 2011, the average physician fee for a buttock implant was \$4,283 and for a buttock lift was \$4,694 versus the reported rates of \$500 to \$1,600 for injections of impure silicone by nonphysicians [30].

A study that included over 200 transwomen concluded that 16.7% of the San Francisco MTF transsexual community had used injected fillers [29]. Owning/renting or living with a partner/family/friend, having had and planning to have surgery in the future, and having used non-prescribed hormones were all significantly associated with filler use. HIV infection was not associated with filler use [29]. Quantifying the use of illicit fillers by transwomen is difficult owing to the lack of epidemiologic data associated with its use. Nonprobability-based studies of transwomen found sample prevalence rates of 25% in Washington, DC, and 33% in Los Angeles, however, such studies were done more than a decade ago [29].

Illicit “silicone” is sometimes obtained at “pumping parties” where a non-professional injects filler material purported to be silicone into areas such as the buttocks, hips, or breasts. Volume of injections varies, but large quantities exceeding 8 or more liters are not uncommon in order to obtain a desired feminized figure [29, 33-35]. Product purity and potential side effects are not always disclosed. Often, industrial-grade as opposed to medical grade silicone is used. There have been reports of injected material consisting of liquid paraffin, petroleum jelly, lanolin, beeswax, flax oil, linseed oil, olive oil, tire sealant, cement glue, and automobile transmission fluid [29-30, 33-34]. The most common sites of injection include the breast, face, buttocks, and hips [29].

Medical grade silicone is standardized with respect to particle purity and viscosity. When employing a sterile, micro-aliquot technique, the risk for serious adverse events from silicone filler injections appears to range between less than 1% to 3% [31-32, 36-37]. Media attention and case reports have illustrated many unfortunate and wide-ranging complications of filler injections including granulomas, nodules, lymphedema, and migration of liquid silicone [36, 38]. Complications may become clinically apparent within days of injection, but may also remain silent until several years post injection.

Table 1. Complications associated with illicit filler injections and suggested treatment

Complications associated with illicit filler injections [30]	
Hours	Arterial occlusion, focal necrosis (related to venous occlusion), post-injection papules, discoloration of the skin, post-injection pain, redness, ecchymosis, bleeding, and swelling and hypersensitivity reactions
Days to weeks	Pain, ecchymosis, pigmentation, inflammatory nodules, pruritus
Months to years	Inflammatory nodules, silicone granulomata cellulitis with sterile abscesses
Suggested Treatment [30]	
<p>First line therapy Antibiotics (minocycline 100mg PO BID or tetracycline 500mg PO BID) for 4-6 weeks – targets delayed inflammatory nodules, granulomas, and sterile abscesses</p> <p>All patients should be considered for surgical excision, if nodules are well circumscribed, and clear margins exist to ensure feasible removal. Surgical consult is recommended.</p> <p><u>Refractory therapy</u> NSAIDs (Celecoxib) may be added to antibiotic therapy to dampen granulomatous inflammatory reaction</p> <p><u>Intralesional steroids (eg intralesional kenalog, intralesional triamcinolone) - used if refractory to 4-6 weeks of antibiotic therapy</u></p> <p>Novel therapy (information largely based on case reports) Imiquimod – antiproliferative effect may play a role in treatment of siliconoma formation Etanercept – 25-50mg SQ twice a week reported to be successful in several case reports Tacrolimus – 0.8-1.0 mg/kg PO BID successful in a small case series Allopurinol – 300mg PO daily, inhibits granuloma formulation by targeting xanthine oxidase; successful in one case report</p>	

Though the incidence of illicit filler complications is low, dermatologists should be able to recognize the syndrome owing to its potentially life threatening nature. Dermatologists must be aware of the epidemiologic, economic, and community-based factors which may drive a transgender patient to seek out such “treatment.” Supportive relationships and partnership formation with transgender patients early on may be preventative.

Post surgical care

MTF transsexuals who have decided to obtain sex reassignment surgery may present with hypersensitivity in the neovaginal region. A case report of a squamous cell carcinoma arising from a neovagina of a MTF transsexual has been reported in the literature, highlighting the importance of full body skin exams in this population [39]. Dermatologists may be called upon to assist with scar revisions in all forms of sex reassignment, including breast implantation (MTF), breast removal (female-to-male), and phalloplasty, which is the surgical creation of a penis. Post surgery, dermatologists must ensure examining both the surgical site, and any donor graft sites (donor grafts used for phalloplasties are most often derived from the forearm). The forearm donor site is often left with an undesirable scar, which may require assessment from a dermatologist or plastic surgeon for scar revision procedures, such as laser treatment. More recent surgical techniques have used the anterolateral thigh flap as a donor site [40].

A long-term evaluation of donor-site morbidity after radial forearm flap for phalloplasty in 44 trans men showed that while 47% were either very satisfied or satisfied with scar appearance at the forearm donor site, 19% were unsatisfied and 5% were very unsatisfied with the scar appearance. The study did not address what specific aspects of scar appearance lead to dissatisfaction or

whether dissatisfied patients sought out dermatologic consultation for scar revision. However, this may be a foreseeable reason for trans men to seek dermatologic care [41]. Scar revision, in general, may lead to consultation from a cosmetic dermatologist for laser treatment. In a retrospective cohort analysis of subcutaneous mastectomies in 202 trans men, 12.6% had undergone scar revision procedures [42]. A pilot study on breast reduction surgery scars (non-transgender individuals) suggested that short-pulsed dye laser and long-pulsed dye laser are equally effective in the improvement of post surgical hypertrophic scars [43]. A case of pyoderma gangrenosum occurring on a scar seven years after breast reduction surgery has been reported in the literature, and should be noted as a rare yet potential dermatologic complication following such surgery [44].

Other common post-surgical issues affecting MTF transgender individuals are urologic, and include rectal vaginal fistulas, vaginal stenosis, and urethral stenosis [45].

Recommendations for the dermatologist

Little evidence exists to guide dermatologists on the care of the transgender patient. This review article serves as a starting point. Key recommendations include:

- Understanding the common dermatologic concerns of transgender patients (see table 2 for summary).
- For MTF transgender patients, facial hair removal (along with hair removal in other parts of the body) may be a chief concern. Hair removal is regarded as extremely vital to assimilation, and is often one of the initial therapies pursued during the transition process.
- A discussion on acne is warranted particularly for FTM transitioners, and should be discussed early on. A dermatologist should describe the effects of testosterone administration on FTM patients, and should monitor for the development of acne and androgenic alopecia.
- If acne is to develop, a dermatologist should be prepared to offer standard treatment regimens (with the likely exception of hormonal therapies, which may counteract the desired effects of testosterone). Acne scarring may also be of concern among patients who have used testosterone for years.
- Dermatologists must continue to perform high quality, full body skin exams, paying close attention to acne, skin dryness, complications from hair-removal procedures, or surgically manipulated tissue (and if applicable, both donor and recipient sites). Patients undergoing hormone replacement therapy (MTF) may have an increased risk of developing both melanoma and nonmelanoma skin cancers. Breast cancer in residual breast tissue may still occur in FTM transgender patients, and must not be overlooked.
- Dermatologists must understand the epidemiologic risk factors associated with transgender individuals, and as with all patients, remain alert for any skin manifestations of HIV (in those with high risk practices), or injected filler use. Remaining open and supportive may play a preventative role.
- Dermatologists should note that many key principals of transgender skin care correlate to medical conditions in the non-transgender community. Examples include skin issues related to: antiandrogen-therapy in prostate cancer patients (similar physiology as MTF transwomen), post surgical skin care after genital reconstruction (ie, in patients with trauma, or those receiving reconstructive surgery for congenital malformation of the genitalia), and acne resulting from hyperandrogen states or androgen producing tumors.
- Dermatologists must provide an overall supportive environment for patients undergoing the transition process, or for those who have completed it. Dermatologists may be asked to communicate or coordinate care with a transgender patient's multidisciplinary team, which may include plastic surgery, endocrinology, urology, gynecology, and/or psychiatry.

Table 2. Dermatologic Issues Affecting Transgender Patients

Dermatologic Issues Affecting Transgender Patients	
Male-to-Female	Female-to-Male
<ul style="list-style-type: none"> -Cutaneous manifestations from estrogen therapy, including xerosis, brittle nails, and possible increased risk of melanoma and nonmelanoma skin cancers -Hair removal techniques (and associated cutaneous side effects) -Skin related issues from breast augmentation, genital reassignment (scarring, possible increased risk of neoplasm) -Illicit filler injection use, with cutaneous and systemic manifestations - HIV-related dermatologic manifestations 	<ul style="list-style-type: none"> -Acne associated with testosterone therapy -Acne scarring associated with testosterone therapy -Androgenic alopecia -Skin related issues related to breast reduction surgery, phalloplasty (scarring, possible increased risk of neoplasm) - HIV-related dermatologic manifestations

CONCLUSION

The complex needs of the transgender population span multiple areas of health and call upon expertise in the realms of hormonal, surgical, and cosmetic therapy. A continued expansion of such knowledge is fundamental toward the improvement of healthcare disparities associated with transgender individuals. This article highlights many understudied areas which the authors hope may be addressed in further studies. Particular areas that may be of benefit include observational studies centered upon acne severity and treatment in trans men, comparative studies on differing methods of hair removal in trans women, and long term dermatologic sequela associated with genital and breast surgery.

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