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Navigating the Intersection of Hormonal Therapy and Acne Management in Trans Youth

Jacquelyn Berman[1], Elena Myalo[2], Darianne Zimmer[3], Travis Jackson[4], Allison Liu[5], Ceilia Severini[6], Ryan Murphy[7], Julia Vinagolu-Baur[8*]

[1,6]*Still University School of Osteopathic Medicine in Arizona, Mesa, AZ*

[2]*Lake Erie College of Osteopathic Medicine, Erie, PA*

[3]*University of California, Riverside School of Medicine, Riverside, CA*

[4]*University of Missouri School of Medicine, Columbia, MO*

[5]*Texas Woman's University, Denton, TX*

[7]*Philadelphia College of Osteopathic Medicine, Philadelphia, PA*

[8]*Norton College of Medicine, SUNY Upstate Medical University, Syracuse, NY*

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Corresponding Author:** ***Julia Vinagolu-Baur, *Norton College of Medicine, SUNY Upstate Medical University, Syracuse, NY*

Abstract

The growing acceptance and recognition of transgender youth seeking medical interventions have prompted dermatologists to consider the implications of prescribing hormonal therapies, such as anti-androgens or estrogens, for acne management. However, the concurrent administration of acne treatments can inadvertently disrupt the delicate balance of existing hormone replacement therapies (HRT), potentially leading to suboptimal outcomes for this vulnerable population. The nuances of hormonal interactions necessitate a comprehensive understanding of how dermatological interventions can affect systemic hormonal levels, particularly in trans youth who may already be undergoing complex and individualized HRT regimens. Prescribing dermatological treatments without considering their potential impact on overall hormonal balance can exacerbate acne or interfere with the goals of HRT, such as gender affirmation and physical comfort. Furthermore, the stigma and mental health challenges faced by trans youth can complicate their adherence to treatment plans, necessitating a collaborative, interdisciplinary approach among dermatologists, endocrinologists, and mental health professionals. Emphasizing open communication and tailored treatment strategies can enhance the effectiveness of acne management while supporting the holistic health and well-being of trans youth, ultimately fostering an environment where dermatological care is both affirming and scientifically sound.

1. Introduction

Acne vulgaris is a chronic inflammatory skin disorder involving multiple pathogenic mechanisms, including hyperseborrhea, follicular hyperkeratinization, microbial dysbiosis, and aberrant immune responses. Excessive sebum production, driven by androgens such as testosterone, combines with desquamated keratinocytes to occlude the pilosebaceous unit. This creates an environment conducive to the proliferation of *Cutibacterium acnes* (*C. acnes*), a bacterium central to acne development [1,2]. This interaction triggers localized inflammation, resulting in acne lesions that range from non-inflammatory comedones to severe nodulocystic forms. Adolescents are particularly affected due to the hormonal surges that increase sebaceous gland activity and alter the follicular milieu [3]. Hormonal acne frequently presents in areas of high dihydrotestosterone sensitivity, such as the chin, jawline, and lower face. However, for transgender youth undergoing exogenous androgen therapy, acne may manifest more severely, with lesions extending to the chest, back, and upper arms [4].

This connection between hormonal fluctuations and acne severity highlights the need for tailored

interventions that consider individual hormonal contexts.

The role of the cutaneous microbiome in acne pathogenesis is equally critical. This complex ecosystem of commensal and opportunistic microorganisms are essential for skin barrier homeostasis, yet adolescence often disrupts this delicate balance [2]. Hormonal fluctuations and environmental stressors characteristic of this developmental stage can lead to microbial dysbiosis, marked by reduced microbial diversity and an overrepresentation of pro-inflammatory *C. acnes* strains [5]. This dysbiosis activates innate immune pathways, including toll-like receptors (TLRs) expressed on keratinocytes and immune cells, which recognize microbial components. TLR activation triggers a cascade of inflammatory mediators, including interleukin (IL)-1β, IL-6, and transforming growth factor beta, that perpetuate immune cell recruitment and amplify chronic inflammation [1]. Over time, this persistent inflammatory state not only exacerbates acne lesions but also contributes to post-inflammatory hyperpigmentation and scarring. Adolescents often worsen this process through mechanical manipulation, such as aggressive "pimple popping" or the application of ineffective remedies popularized on social media, like toothpaste on lesions. These practices not only fail to address the underlying causes of acne but further irritate the skin, increasing the risk of prolonged inflammation and long-term damage.

Beyond biological factors, lifestyle and environmental influences significantly affect acne development and severity. Common contributors include a Western diet, poor sleep hygiene, cosmetic use, and stress, with these factors often intertwined with behavioral habits unique to adolescence [6]. Socioeconomic disparities also play a role, with studies showing that individuals seeking dermatological care for acne are predominantly from urban areas with higher socioeconomic status [6]. This disparity in access to care can lead youth from lower-income backgrounds to rely on over-the-counter treatments. Unfortunately, these products often lack the potency needed for severe acne cases, leaving many adolescents without adequate relief. These barriers to care highlight the importance of accessible and equitable treatment strategies that address these gaps. For transgender adolescents, these challenges are compounded by the potential interaction between acne treatments and hormone replacement therapy, as well as by the stigma and misgendering in healthcare settings [7]. The unique needs of this population call for affirming care environments that recognize the interplay between dermatological and psychological factors.

The psychological toll of acne can be profound particularly during adolescence, when physical appearance significantly influences social interactions and self esteem. The visibility of acne lesions often exacerbates feelings of anxiety, depression and low-self worth [8]. For transgender youth, these effects may be highlighted by the additional mental health challenges associated with gender dysphoria and discrimination. Studies have linked acne to heightened risks of depression and suicidal ideation, particularly amoung sexual minority youth [9]. These biological and psychosocial factors make acne particularly burdensome for transgender youth, underscoring the need for research, education, and treatment approaches tailored to this marginalized population.

2. Management of Acne

Acne vulgaris affects over 85% of adolescents worldwide, making it one of the most common dermatological conditions in this age group [10]. Given the condition's multifactorial pathogenesis, treatment of acne can be complex, often targeted with a combination of topical and systemic therapies tailored to disease severity. Accurate classification of acne severity is essential for guiding treatment decisions and monitoring therapeutic outcomes. Among the various grading systems available, the Investigator Global Assessment (IGA) scale is widely used due to its simplicity and reliability in clinical settings [11]. This scale evaluates acne severity using a 5-point ordinal system, ranging from 0 (clear) to 4 (severe), and considers factors such as lesion count, distribution, dyspigmentation, and scarring. Its widespread adoption in both routine practice and randomized controlled trials underscores its role as a practical tool for standardizing assessments and facilitating communication between clinicians and patients. By enabling consistent and objective grading, the IGA scale supports the development of personalized treatment plans that address both the physical and psychosocial burden of acne.

2.1. Topical Therapies

Topical agents form the cornerstone of initial management and include retinoids, benzoyl peroxide, salicylic acid, azelaic acid, and antibiotics. Retinoids, such as adapalene,

tretinoin, and tazarotene, modulate keratinocyte differentiation, reduce follicular occlusion, and exhibit powerful anti-inflammatory properties, making them effective in managing comedonal acne [12]. A randomized trial of 207 patients demonstrated that 0.025% tretinoin reduced acne lesions by 63% over three months, highlighting its efficacy [13]. However, topical retinoids may cause side effects such as erythema, dryness, pruritus, and photosensitivity, necessitating concurrent sunscreen use. Among these, tazarotene demonstrates the greatest efficacy, but is associated with higher rates of irritation compared to adapalene. Benzoyl peroxide is another widely used agent, known for its bactericidal activity against *C. acnes* and its ability to minimize resistance when combined with topical antibiotics such as clindamycin or erythromycin [14]. Although benzoyl peroxide may cause dryness and irritation, its safety during pregnancy and ease of use make it a versatile option. Moreover, while salicylic and azelaic acids are useful as components of treatment plans, studies have suggested these agents are more effective for post-inflammatory hyperpigmentation.

2.2. Systemic Therapies

For inflammatory lesions or moderate to severe acne, systemic therapies such as oral antibiotics, isotretinoin, and hormonal treatments are employed. Doxycycline and minocycline, first-line oral antibiotics, primarily reduce *C. acnes* colonization and inflammatory cytokine production but are contraindicated in pregnant individuals and children under eight due to the teratogenicity and risk of dental discoloration. Of note, sarecycline, a newer narrow-spectrum tetracycline, has been shown to improve both inflammatory and noninflammatory lesions with fewer gastrointestinal side effects compared to alternative tetracyclines [15]. For nodular or recalcitrant acne, isotretinoin–an oral retinoid–directly suppresses sebaceous gland activity and sebum production. Despite its efficacy, significant side effects include teratogenicity, hyperlipidemia, cheilitis, and xerosis [16]. Given this, routine laboratory monitoring is necessary prior to and while undergoing therapy.

2.3. Hormonal and Anti-Androgen Therapies

The use of hormonal and anti-androgen therapies in managing acne requires careful patient selection, particularly in cases where androgen excess plays a significant role. Persistent acne may result from either elevated circulating androgens or an increased sensitivity of the pilosebaceous unit to androgenic stimulation [17]. Hormonal treatments, such as oral contraceptives, estrogens, and anti-androgens, are particularly effective in addressing these underlying mechanisms. Anti-androgens like cyproterone acetate and spironolactone act as competitive inhibitors of the dihydrotestosterone receptor, effectively blocking androgen activity. This inhibition also suppresses the production of follicle-stimulating hormone and luteinizing hormone, leading to decreased androgen levels. Spironolactone, a non-selective mineralocorticoid receptor antagonist, is widely used for androgen-mediated acne, as it reduces sebaceous gland activity and sebum production, making it especially effective for cisgender females with persistent acne [18]. However, spironolactone is contraindicated in cisgender males and transmasculine individuals undergoing masculinizing hormone therapy, as it can induce feminizing side effects, such as gynecomastia and menstrual irregularity. Transfeminine individuals, on the other hand, benefit significantly from the combined use of anti-androgens like spironolactone and estrogen therapy, which inhibit sebaceous gland activity and alleviate acne, aligning with their gender-affirming goals [4]. Conversely, testosterone therapy in transmasculine patients often exacerbates acne, with prevalence rates rising from 6.1% to 31.1% post-therapy [19]. This underscores the need for tailored acne management strategies that account for the unique hormonal milieu and psychological well-being of transgender patients.

3. Hormone Replacement Therapy

Hormone replacement therapy (HRT) is an essential component of gender-affirming care, designed to align physical characteristics with a patient's gender identity. For transgender men, HRT typically involves exogenous testosterone, which promotes masculinization through virilizing effects such as increased muscle mass, facial and body hair growth, and voice deepening. Testosterone exerts its effects by binding to androgen receptors in tissues like the skin, muscles, and brain, initiating gene expression that leads to these physical changes [4]. Conversely, transgender women use exogenous estrogen, often in combination with anti-androgen medications, to suppress androgenic effects and enhance feminization. Estrogen primarily acts through central hormonal pathways, inhibiting gonadotropin secretion from the anterior pituitary, thereby reducing androgen levels [20]. This reduction mitigates

masculine features such as body and facial hair while promoting breast development. In many cases, estrogen alone may not be sufficient in achieving the desired effects, so anti-androgen medications are often utilized to enhance these changes [21]. Therefore, a combination of treatments is often necessary to achieve optimal effects in transgender women.

The primary goal of hormone replacement therapy is to improve alignment between an individual's physical appearance and gender identity, significantly enhancing quality of life [22]. This intervention addresses the often profound disconnect transgender individuals may feel between their gender identity and biological sex. For transgender men, testosterone therapy induces masculinizing changes such as increased body hair, muscle mass, and voice deepening. Conversely, estrogen therapy for transgender women promotes feminization, including breast development and fat redistribution [23]. In addition to its physical effects, HRT offers substantial psychological benefits. Studies have shown that transgender individuals undergoing HRT experience improved mood, sexual function, and overall well-being, with reductions in both psychological distress and gender dysphoria [22]. For transgender youth, these effects are particularly profound, as HRT can help alleviate the mental health challenges associated with gender incongruence, such as depression and anxiety [24]. These improvements in mental health and self-esteem underscore the critical role of HRT in gender-affirming care, addressing the multifaceted needs of this population. However, these benefits are accompanied by potential side effects, which vary based on the type of hormone administered.

In transgender men, testosterone therapy frequently leads to side effects such as increased body hair, male-pattern hair loss, and acne. Testosterone's role in stimulating sebum production is a primary factor exacerbating acne, a common concern for transgender youth undergoing HRT [25]. For transgender women, estrogen therapy typically promotes feminizing changes. However, these benefits are tempered by the higher rates of bone demineralization observed in transgender women receiving HRT, particularly when anti-androgen medications are included in their regimen [26]. Although exogenous estrogen can help mitigate bone loss, the concurrent use of anti-androgens often exacerbates this issue, necessitating alternative therapeutic strategies to preserve bone health [27]. This underscores the importance of individualized treatment plans to balance feminizing effects with the long-term health risks associated with bone demineralization.

The long-term cardiovascular implications of hormone replacement therapy in transgender youth remain poorly understood, highlighting a critical gap in current research. Evidence suggests that prolonged administration of exogenous testosterone can elevate triglycerides and reduce high-density lipoprotein cholesterol levels, indicating potential metabolic changes [28]. However, these lipid profile alterations have not been definitively linked to increased cardiovascular events, leaving the clinical significance of these findings unresolved. Similarly, the cardiovascular effects of exogenous estrogen are inconclusive, though its association with an increased risk of diabetes may indirectly heighten the likelihood of future cardiac complications [29]. These uncertainties necessitate comprehensive cardiovascular monitoring for transgender individuals receiving hormone replacement therapy, emphasizing the importance of proactive risk management in this population.

3.1. Interaction between Acne management and Hormone Replacement Therapy

The intersection of hormone replacement therapy and acne development in transgender youth presents unique challenges. Masculinizing therapies, such as testosterone, significantly contribute to hormonal acne, predominantly manifesting in androgen-sensitive areas like the face, chest, back, and upper arms. A retrospective cohort study found that 31% of individuals undergoing testosterone HRT experienced acne as a side effect, underscoring its prevalence in this population [19]. Compounding this issue, chest binders frequently worn by transmasculine individuals for gender affirmation can exacerbate acne through mechanical irritation, prolonged skin occlusion, and increased sweat accumulation. In contrast to testosterone-based HRT, which can stimulate sebum production and increase inflammation, feminizing HRT frequently reduces acne due to the antiandrogenic effects of estrogen therapy, which inhibits androgen activity and decreases sebum production [4]. These contrasting effects underline the importance of tailored acne management strategies that account for the specific hormonal regimens used.

Managing acne in transgender youth undergoing hormone replacement therapy is further complicated by the potential contraindications

between common acne therapies and hormone treatments. Many first-line acne medications, including oral contraceptives and spironolactone, are unsuitable for transmasculine individuals as they counteract the effects of testosterone [4]. For instance, spironolactone, commonly used for its antiandrogenic properties in acne treatment, could negate the masculinizing effects of testosterone therapy. Similarly, oral contraceptives, which regulate hormonal imbalances, may conflict with masculinizing hormone goals. This overlap between acne treatment and HRT highlights the need for alternative therapeutic strategies that prioritize hormonal alignment while effectively addressing acne.

Non-hormonal therapies provide a critical pathway for managing acne in transgender youth without interfering with HRT. Current non-hormonal acne treatments include topical retinoids, benzoyl peroxide, antibiotics, salicylic acid, and azelaic acid, with retinoids being among the most widely used therapies. These topical treatments form the cornerstone of acne management, serving as both initial and maintenance therapy. They can be used as monotherapy (excluding topical antibiotics) or in combination with other medications to enhance efficacy [11]. Benzoyl peroxide, known for its antibacterial, anti-inflammatory, and keratolytic properties, also regulates sebum production, making it an effective option. Similarly, salicylic acid, a beta hydroxy acid, exfoliates the skin and provides keratolytic and anti-inflammatory effects, while azelaic acid, a dicarboxylic acid, offers antibacterial and anti-inflammatory benefits. Retinoids, derived from vitamin A, work by reducing sebum production, decreasing inflammation, and promoting skin cell turnover. These agents are available in both topical and oral formulations, including isotretinoin.

Isotretinoin, in particular, has demonstrated significant efficacy in treating acne among transgender individuals undergoing masculinizing hormone therapy. In a study by Choe et al., 48 of 55 patients treated with isotretinoin experienced notable improvement in acne, and 26 achieved complete clearance [30]. Higher cumulative doses yielded even greater success, with 32 of 33 patients showing improvement, including 21 achieving full clearance. These findings underscore isotretinoin's potential as a highly effective non-hormonal acne treatment for this population, offering benefits without interfering with testosterone therapy. While benzoyl peroxide, salicylic acid, and azelaic acid have not been specifically studied in transgender youth, their non-hormonal nature suggests they are likely safe and effective in this population. Further research into these treatments' use among individuals undergoing hormone replacement therapy would provide valuable insights and inform clinical best practices.

4. Barriers to Care And Social Stigma

Building trust and a trans-affirmative environment are pivotal in mitigating the stigma and healthcare avoidance often encountered by transgender individuals. Studies indicate that 22.8% of transgender adults avoided healthcare due to anticipated discrimination [31]. Such avoidance is not solely attributable to overt prejudice but often stems from subtle biases, microaggressions, and inadequate provider training, all of which undermine patient trust. For transgender youth, who may already grapple with societal stigma and identity validation, these barriers are further exacerbated by the added vulnerability of adolescence. Distrust between patients and providers frequently arises when healthcare settings fail to respect patients' gender identities, as evidenced by misgendering, the use of incorrect pronouns, or dismissive attitudes toward their concerns. These experiences create an environment where transgender youth feel alienated, discouraging them from seeking care, including dermatological and hormonal therapies critical for managing conditions like acne.

Structural constraints to healthcare access further complicate the issue. Research reveals that transgender men experience higher levels of healthcare avoidance than transgender women, with non-binary/genderqueer individuals facing greater reluctance than both [31]. The transgender population also experiences higher rates of poverty (28.8% compared to 13.5% of the general population, which exacerbates healthcare access challenges [31]. Financial constraints, lack of insurance coverage for gender-affirming treatments, and geographic disparities further restrict access to specialized providers. Furthermore, many transgender individuals conceal their identity, resulting in missed opportunities for preventative care [31].

Trust between medical providers and patients is essential for individuals to disclose their gender identity, which underscores the need for trans-affirmative policies, inclusive language, and a welcoming environment within healthcare organizations.

Fear of discrimination plays a significant role in healthcare avoidance, which is further highlighted by a community-based survey involving 417 transgender individuals. The study found that individuals who delayed care due to fear of discrimination were three times more likely to experience depression and suicidal ideation, and four times more likely to have attempted suicide in the past year [32]. This underscores the importance of creating inclusive environments that reduce fear and encourage trust between patients and providers. Inadequate provider knowledge of transgender-specific healthcare needs exacerbates these issues. For example, transgender men face inadequate pelvic health screenings, and transgender women have limited access to breast tissue screenings, contributing to unmet healthcare needs [33]. To address these gaps, inclusive intake forms, nondiscriminatory policies, and staff training on inclusivity are crucial in building trust and ensuring positive patient-provider interactions.

A systematic review of 41 articles examining healthcare disparities among transgender individuals highlighted additional concerns, such as HIV prevention challenges, exclusion from clinical trials, and inadequate cholesterol screening guidelines [33]. Transgender women, for instance, exhibit higher rates of HIV, yet face significant barriers to preventative care. Similarly, transgender men have lower rates of adequate Pap tests, which is especially concerning given the high rates of condomless receptive sex in this population. These gaps in care are compounded by the lack of research into breast/chest tissue screenings, flu shot uptake, and colorectal screenings for transgender patients. Further research into preventive healthcare guidelines is essential to improve medical care and treatment outcomes for the transgender population.

A multidisciplinary approach to care is crucial for transgender youth dealing with conditions like acne. Dermatologists, endocrinologists, and mental health providers each play a vital role in addressing both the physical and psychological aspects of acne treatment. Dermatologists focus on diagnosing and treating acne, while endocrinologists manage hormone therapy, which significantly impacts skin health [34]. Mental health providers are crucial for evaluating the psychological aspects of transitioning, providing ongoing support. By integrating these specialties into a collaborative care model, healthcare teams can ensure comprehensive and effective treatment that meets the diverse needs of transgender youth.

To enhance care, dermatology practices must foster a safe and inclusive environment for transgender patients, who often experience heightened insecurity about their appearance. Unfortunately, skin conditions in this population are frequently underdiagnosed and underrecognized, which worsens their impact on quality of life [35]. This gap in care can lead to the progression of conditions, ultimately requiring more aggressive treatments that could have been avoided with earlier intervention. Current hormonal therapies can sometimes worsen conditions like acne or male-pattern hair loss, and clinical trials for acne treatments often exclude transgender participants, leaving gaps in the data [35,36]. Future research must prioritize the inclusion of transgender patients in clinical studies to better understand how hormonal treatments influence acne outcomes. However, challenges such as funding and the inclusion of transgender patients in programs like iPLEDGE, which often categorize them ambiguously, must be addressed [37]. With a more inclusive, patient-centered approach, transgender youth can receive the best possible care for acne and related conditions, but continued efforts are necessary to close these gaps in research and healthcare access.

5. Conclusion

The management of acne in transgender youth represents a pivotal intersection of dermatological care, endocrinology, and gender-affirming medicine. Acne, a condition that already imposes significant physical and psychological burdens, is further complicated by the hormonal dynamics introduced by hormone replacement therapy (HRT). Testosterone therapy in transmasculine individuals often exacerbates acne, while feminizing regimens tend to alleviate it, highlighting the necessity for individualized, hormone-informed approaches. Conventional acne treatments must be carefully selected to avoid undermining the effects of HRT, requiring non-hormonal alternatives or highly tailored therapeutic strategies that balance dermatological outcomes with gender-affirming goals. Effective acne management extends beyond the skin's surface. Transgender youth frequently face compounding psychosocial challenges, including stigma, discrimination, and limited access to affirming care, which heighten the barriers to successful treatment. Addressing these complexities demands a multidisciplinary

approach that integrates dermatological expertise with endocrinological oversight and mental health support. Such collaboration ensures that treatment plans are not only effective but also attuned to the diverse physical, emotional, and psychological needs of transgender youth.

Furthermore, fostering inclusive healthcare environments that prioritize trust and open communication is crucial to encouraging adherence and improving outcomes. By recognizing the unique hormonal influences, psychosocial stressors, and mental health burdens faced by this population, healthcare providers can craft patient-centered care that promotes well-being and self-esteem. Looking ahead, research must prioritize the inclusion of transgender individuals in clinical trials to develop evidence-based guidelines that truly reflect their needs. The commitment to culturally competent, affirming care will transform dermatological practices, allowing them to evolve into a model of precision medicine that embraces the broader goals of gender affirmation. Through these efforts, dermatological care can not only improve acne outcomes but also contribute meaningfully to the overall health, identity congruence, and quality of life for transgender youth.

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