GENERAL GYNECOLOGY

Care of the transgender patient: the role of the gynecologist

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Gender dysphoria refers to distress that is caused by a sense of incongruity between an individual's self-identified gender and natal sex. Diagnosis is made in accordance with the *Diagnostic and Statistical Manual of Mental Disorders* and treatment first involves psychiatric therapy, which can help determine a patient's true goals in regards to achieving gender identity. Patients who wish to transition to the opposite sex must undergo a supervised real-life test and often are treated with hormonal therapy to develop physical characteristics consistent with their gender identity. Sex reassignment surgery is an option for patients who wish to transition completely. Transpatients face many barriers when it comes to basic health needs including education, housing, and health care. This is a result of long-standing marginalization and discrimination against this community. Because of these barriers, many patients do not receive the proper health care that they need. Additionally, because of certain high-risk behaviors as well as long-term hormonal therapy, transpatients have different routine health care needs that should be addressed in the primary care setting. Gynecologists play an important role in caring for transgender patients and should be knowledgeable about the general principles of transgender health.

Key words: gender dysphoria, gender identity disorder, sex reassignment, transgender, transsexual

Gender identity is the sense one has of being male or female.[1] Transgender individuals are people who feel an incongruity between their self-identified gender and their birth gender.[2] Manifestation of transgenderism exists on a spectrum. Patients may simply live their lives as members of the opposite sex, they may choose to undergo partial transition with hormonal therapy and/or some minor physical changes, or complete the transition with genital reassignment surgery.

About two-thirds of transgender individuals have early onset of identification with the opposite sex in early childhood, while a third of patients discover their identity later in life.[3] Understanding proper terminology is an important part of the diagnostic stage, as historically, there has been muddling of certain terms. Psychiatric diagnoses in the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) for conditions that relate to gender identity and sex behaviors have always been very controversial. It was not until the 1940s that a distinction was made among the terms "transgenderism," "transsexualism," and "homosexuality." "Transgenderism" was used to describe individuals who identified with the opposite sex and desired to live their lives in that role; while "transsexualism" was specific to individuals desiring complete transition through sex reassignment.[4] However, "transsexualism" did not appear as a formal diagnosis in the *DSM* until 1980,[5] 7 years after "gender dysphoria" was introduced as a standard psychiatric term.[6] In 1994, "transsexualism" was removed from the *DSM* and replaced with "gender identity disorder," a term used to diagnose patients who experience significant gender dysphoria and wish to live their lives as the opposite sex.[7] The *DSM-V*, published in May 2013, revised their diagnostic criteria for patients experiencing gender incongruence. In an attempt to depathologize gender identity and to eliminate some of the social stigma attached to it, "gender identity disorder" was removed from the *DSM* as a formal psychiatric diagnosis, and it was replaced with "gender dysphoria," which refers to the distress that is caused by a discrepancy between a person's gender identity and natal sex. This new diagnosis attempts to avoid classifying patients who may vary in their gender identity or expression with an actual psychiatric condition, and it provides guidelines for diagnosis that will assist providers with treatment to reduce the distress that these patients experience. "Transsexualism" is still used to describe those individuals who wish to or have completed transition with reassignment surgery. "Gender nonconformity" refers to behavior and is the extent to which an individual's expression of gender identity differs from cultural norms for that particular gender. The most important thing to realize is that while there are subtle distinctions among "gender nonconformity," "transgenderism," and "transsexualism," any of these conditions or forms of expression can be associated with gender dysphoria, which implies distress in an individual's life, and can be treated with a combination of psychotherapy, hormonal therapy, and surgery.[8] Figure 1 lists the different terms and their definitions commonly used to describe gender identity and sex behaviors.

Large epidemiologic studies on the incidence and prevalence of transgenderism have not been conducted, as this population has proven to be very

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difficult to study. The only data available are on the prevalence of individuals who present for sex reassignment or gender-related care in Europe. A study from The Netherlands reported a prevalence rate of 1:11,900 and 1:30,400 in men and women, respectively.[9] In Europe, this 1:3 ratio of women to men is common, perhaps because it is easier for women to assume masculine roles in these societies without having to seek sex reassignment, whereas assuming a feminine role for men is less accepted. However, in other parts of the world, small studies have revealed that there are as many, if not more, women than men who are transgender.[10] Therefore, no definitive conclusions can be drawn regarding the actual prevalence between the 2 sexes.

The etiology of transgenderism is not known. A biological theory supports the concept of sexual differentiation in the brain and relies on the notion that the human brain is dimorphic in nature and in utero develops into either the female or male brain.[11] Cadaver studies examining male-to-female transsexual brains have shown a female-specific pattern of development and size specifically in the bed nucleus of the stria terminalis, which is responsible for sex behavior.[12] Interestingly, the size of this bed nucleus was shown to be independent of sexual orientation and only correlated with biologic sex.[13] These limited data imply that there may be an inherent biologic component to gender identity, but this theory requires further research.

While there were once strong beliefs that transgenderism was purely psychiatric in nature,[11] there is no evidence currently that this is the case. Additionally, theories exist regarding the role of the environment and child rearing, but there are not enough data to conclude that this plays a major role in the disorder either. As previously mentioned, there have been efforts recently to "depsychopathologize" conditions related to gender nonconformity and identity. In 2010, the World Professional Association for Transgender Health (WPATH) released a statement addressing this, stating the following: "the expression of gender characteristics, including identities that are not stereotypically associated with one's assigned sex at birth is a common and culturally diverse human phenomenon [that] should not be judged as inherently pathological or negative." The organization emphasizes that gender nonconformity is simply a matter of diversity while gender dysphoria may require treatment as the individual's feelings of discrepancy between natal sex and gender identity may cause significant distress.[14] Only some individuals with gender nonconformity experience gender dysphoria and it is crucial to understand that while this is mislabeled as a psychiatric disorder, the actual etiology is multifactorial, and should simply be considered a variant of what society may consider to be normal.

FIGURE 1
Terminology

Sex: Biological and physiological characteristics that define "men" and "women" without regard to one's own identity.

Gender identity: Inherent sense of being male or female regardless of sex.

Sexual orientation: The sex that a person is physically attracted to; also known as ***sexual preference***.

Gender nonconformity: The extent to which a person's gender identity, role, or expression differs from the cultural norms prescribed for people of a particular sex.

Transgenderism: Individuals who identify with the opposite sex rather than their natal sex, who have not achieved reassignment to the desired sex or want only partial adaptation.

Transsexualism: Individuals who desire to achieve reassignment and have committed to transitioning to their desired sex.

Transvestitism: Individuals who have a preference for cross-dressing but have no desire to change their biologic sex.

Gender dysphoria: Discomfort or distress that is caused by a discrepancy between a person's gender identity and that person's natal sex. Current formal diagnosis found in the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition).

Gender identity disorder: Previous formal diagnosis found in the *Diagnostic and Statistical Manual of Mental Disorders* (4th edition) for individuals who experience gender dysphoria; these individuals can be transgender or transsexual.

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Diagnosis and initial management

The standards of care and treatment for patients with gender dysphoria have been established by 2 important organizations: the WPATH (formerly the Harry Benjamin International Gender Dysphoria Association) and the Endocrine Society. The first Standards of Care for Gender Dysphoric Persons was drafted in 1978 with the most recent version (7th edition) published in 2011.[14] While these standards are flexible to meet the needs of all transgender individuals, they offer a framework for providers to care for these patients.

An important goal of WPATH has been "lasting personal comfort with the gendered self to maximize overall psychological wellbeing and self-fulfillment."[1] Individuals who experience gender dysphoria must be properly evaluated before this goal can be achieved, and this evaluation takes place in 2 parts. First, the criteria put forth by the *DSM* must be met (Figure 2). This is determined by a trained mental health professional who is competent in the care of transgender patients and understands his or her role in the care of these patients, as outlined by the WPATH standards of care. Once patients are determined to meet criteria for gender dysphoria, a period of up to 12 months is sometimes necessary to assess the

FIGURE 2
DSM diagnostic criteria for gender dysphoria

A. A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months duration, as manifested by 2 or more of the following indicators:

1. A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or, in young adolescents, the anticipated secondary sex characteristics)

2. A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or, in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics)

3. A strong desire for the primary and/or secondary sex characteristics of the other gender

4. A strong desire to be of the other gender (or some alternative gender different from one's assigned gender)

5. A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender)

6. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender)

B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning, or with a significantly increased risk of suffering, such as distress or disability

Subtypes

- With a disorder of sex development
- Without a disorder of sex development

DSM, Diagnostic and Statistical Manual of Mental Disorders, fifth edition.

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severity of the gender dysphoria and to determine if the patient will benefit from a variety of transition processes, including sex reassignment surgery. Additionally, in this stage, patients are assessed for psychiatric comorbidities and treated accordingly. Because of the stigma that is attached to gender nonconformity, prejudice and discrimination often ensues toward this population, which can result in a phenomenon termed "minority stress."[1] This type of social impact and stress can lead individuals to experience debilitating stress and anxiety, and therefore, psychiatric therapy is sometimes necessary to treat any comorbid psychiatric conditions such as depression, anxiety, and posttraumatic stress disorder. During this diagnostic phase, patients are encouraged to participate in the real-life test, which involves an extended period of time (at least 12 months) where the patient lives full time as a person of the desired sex.[14] This experience is imperative for individuals as they learn to interact in the community as their desired sex, and helps them to affirm their decision to move forward with hormonal therapy and surgical reassignment if desired.

As outlined by the 2011 WPATH standards of care,[14] the above-mentioned initial management strategies are important for patients before they proceed with further treatment. The most basic requirement is that patients undergo assessment by a mental health professional, and have well-documented gender dysphoria. To proceed with hormonal therapy, a referral from a mental health provider is important and at least 3 months of the real-life experience is recommended.[15] Most surgical procedures require this referral as well, if not 2 separate referrals, while some procedures require 12 months of continuous hormonal therapy as well as the completion of the real-life experience. Providers managing hormonal therapies and/or performing gender-related surgeries are responsible for ensuring that these requirements have been met. While some providers believe it is important for patients to undergo formal psychotherapy for gender dysphoria, it is not an absolute requirement for hormonal or surgical management.

Hormone therapy

Many transgender patients choose to initiate hormone therapy to help make their physical appearance concordant with their gender identity. The diagnostic phase must be complete prior to initiating hormones and many patients also remain in therapy during this time period. Some patients choose to overlap the real-life experience with hormone therapy, which is encouraged. The main objectives of hormonal therapy are to suppress the sex characteristics associated with the patient's natal sex, and to induce the characteristics of the desired sex. Figure 3 describes the options for hormonal therapy for both male-to-female and female-to-male patients and Figure 4 outlines the standards for monitoring hormonal therapy once it is initiated. Guidelines for initiation and maintenance of hormonal therapy for transgender patients are outlined by the Endocrine Society.[15] The most important step in the initiation of hormonal therapy is to ensure that patients do not have comorbid conditions that could be exacerbated by hormonal treatments. Per the society's guidelines, estrogen therapy should be used with caution, if used at all, in male-to-female patients with history of thromboembolic disease, prolactinoma, significant liver disease, breast cancer, coronary artery disease, and migraine headaches with aura. Similarly, female-to-male patients are at risk for exacerbation of breast or endometrial cancer and significant liver disease while on testosterone therapy.

In male-to-female patients, androgen effects are suppressed with progestational

agents such as progesterone or medroxyprogesterone acetate. In Europe, the most commonly used progestational agent is cyproterone acetate, which is currently not available for use in the United States. Nonsteroidal antiandrogens such as spironolactone and finasteride can be used, as well as the gonadotropin-releasing-hormone analogue leuprolide and gonadotropin-releasing-hormone agonists such as the histrelin implant, commonly used to treat prostate cancer. Feminine characteristics such as breast formation, female pattern of fat distribution with reduction of overall lean body mass, and a reduction in male-pattern hair growth are induced with the use of estrogens.[16] The most commonly used form of estrogen is estradiol, which can be administered orally, intramuscularly, or transdermally. In the past, oral ethinyl estradiol was commonly used, however the doses required to achieve sex reassignment were associated with a high risk of venous thrombotic events,[17] and use of this medication is now avoided. The transdermal route of estrogen administration is highly recommended, as therapeutic effects are achieved at lower peak doses since first-pass hepatic metabolism is avoided, plasma hormone levels remain constant, and the sustained drug delivery reduces the need for frequent self-administration, which improves patient compliance.

The primary objective of hormonal therapy for female-to-male patients is to induce virilization. This is achieved with testosterone therapy. The 2 most commonly used formulations include testosterone enanthate and testosterone undecanoate. Androgen therapy results in increased muscle mass, decreased fat mass, increased facial hair and acne, male pattern baldness, and increased libido.[18] Frequently, testosterone therapy will lead to the suppression of menses, especially if it is administered intramuscularly. If this is not achieved, especially in the case of transdermal testosterone administration, progesterone therapy can be used concomitantly to stop menstrual flow.[15]

Patients who have initiated hormonal therapy report good satisfaction from this treatment. A metaanalysis of 28 observational studies looked at 1833 patients who received hormonal therapies. In all, 80% (69-89%) of patients reported significant improvement in gender dysphoria, 78% (56-94%) reported significant improvement in psychological symptoms, 80% (72-88%) had improvement in quality of life, and 72% (60-81%) stated they had improvement in sexual function.[8] While there are formulations of hormonal therapy that are commonly used to reach the above goals, it is important to note that there are no comparative or randomized studies to test the efficacy and safety of these drugs. Current recommendations for management are based on expert opinion and experience.[15] Continued medical supervision by a trained physician is required during hormone therapy.[19] This is paramount as the prevalence of unsupervised hormone use has been reported to be as high as 58% in male-to-female transgender patients.[20] The Endocrine Society recommends monitoring patients every 3 months during the first year of therapy then once or twice yearly thereafter.[15] At these visits, patients are monitored for metabolic alterations resulting from therapy as well as changes in their quality of life. Documented side effects from these formulations include depression and increased risk of suicidal thoughts, mood swings, hyperprolactinemia, elevated liver enzymes, migraines, and decreased insulin sensitivity.[19,21] All of these changes are important to monitor as they can significantly impair the health of these patients.

FIGURE 3
Hormonal therapy for transsexual patients

Male-to-Female

Estrogen therapy options
- Estradiol 2.0-6.0 mg PO daily
- Estradiol patch 0.1-0.4 mg TD twice weekly
- Estradiol valerate 5-30 mg IM every 2 weeks

Antiandrogen therapy options
- Progesterone 20-60 mg PO daily
- Medroxyprogesterone acetate 150 mg IM every 3 months
- Cyproterone acetate 50-100 mg PO daily[a]
- GnRH agonist (leuprolide) 3.75-7.5 mg IM monthly
- Histrelin Implant 50mg implanted every 12 months
- Spironolactone 100-200 mg PO daily
- Finasteride 1 mg PO daily

Female-to-Male

Testosterone therapy options
- Testosterone enanthate or cypionate 100-200 mg IM every 2 weeks
- Testosterone undecanoate 1000 mg IM every 12 weeks or 160-240 mg PO daily[a]
- Testosterone gel 1% 2.5-10 gm TD daily
- Testosterone patch 2.5-7.5 mg TD daily

IM, intramuscular; *PO*, oral; *TD*, transdermal.

[a]Not currently available in the United States.

Adapted from the Endocrine Society Guidelines, 2009[15] and Spack, 2013.[46]

Sex reassignment surgery

Figure 5 provides an overview of the most commonly performed procedures for transsexual women and men. Male-to-female sex reassignment surgery involves gonadectomy, remodeling of the male external genitalia to create female external genitalia with reconstruction of the urethral meatus and a sensate clitoris, and creation and lining of a neovaginal cavity.[5] The neovagina can be lined using penile and sometimes scrotal skin, nongenital skin flaps, or colonic grafts.[22] While skin grafts are the most commonly used, colonic flaps have been taken from the cecum and rectosigmoid

FIGURE 4
Monitoring of hormone therapy in transsexual patients

Male-to-Female

Evaluate patients every 2-3 months in the first year and then 1-2 times per year thereafter to monitor for appropriate signs of feminization and for development of adverse reactions

Measure serum testosterone and estradiol levels every 3 months
- Serum testosterone levels should be <55 ng/dL
- Serum estradiol levels should be 100–200 pg/dL
- Adjust estradiol dosage according to serum levels

Measure serum electrolytes every 2-3 months for the first year if patients are taking spironolactone

Measure serum prolactin levels at baseline, at 12 months following initiation of treatment, and biennially thereafter

Female-to-Male

Evaluate patients every 2-3 months in the first year and then 1-2 times per year thereafter to monitor for appropriate signs of feminization and for development of adverse reactions

Measure serum testosterone every 2-3 months until levels are in the normal physiologic range (320–1000 ng/dL)[a]
- Testosterone enanthate/cypionate: measure between injections
- Testosterone undecanoate: measure prior to the next injection
- Transdermal testosterone: measure any time after week 1

Measure estradiol levels during the first 6 months of testosterone treatment or until there is cessation of menses for 6 months
- Estradiol levels should be <50 ng/dL

Measure complete blood count and liver function tests at baseline and every 3 months for the first year and then 1-2 times per year thereafter

[a]Because of high sex hormone binding globulin levels in natal women, total testosterone levels may be high while free testosterone levels are normal during the first 9 months of therapy.

Adapted from the Endocrine Society Guidelines, 2009[15] and Spack, 2013.[46]

to create a neovagina that has natural lubrication. While this seems favorable, patients have had problems with excessive mucus production as well as episodes of colitis and intestinal obstruction.[23] For these reasons, local skin flaps remain the preferred method of lining a neovagina in male-to-female reassignment surgery. After 2 years of hormonal therapy, approximately 50% of patients find their breast size adequate and do not seek further enhancement,[21] while those who wish to have larger breasts usually undergo standard breast augmentation. Additional nongenital feminizing operations include chondrolaryngoplasty to reduce the size of the Adam's apple with or without voice surgery to raise the pitch of the voice, facial feminization with rhinoplasty, and body contouring through liposuction and fat redistribution.[5]

Female-to-male patients can undergo bilateral mastectomy, hysterectomy, and bilateral salpingo-oophorectomy. When these patients initially present, there is sometimes hesitancy about the extent of surgery they may need to transition to their desired sex. Although aromatization of testosterone to estradiol could theoretically be a risk factor for endometrial cancer,[24] there are no reported cases of uterine cancer in these atients. However, it is not unreasonable in this patient population to recommend the above surgeries as cancers that develop in these organs are not easily detectable, and so, removal may be beneficial. Additionally, removing the female pelvic organs is helpful in the transition process and helps patients identify with their gender. Those patients who have undergone mastectomy often choose to have chest-contouring surgery as well. After testosterone therapy, approximately 5% of patients find their clitoris to be enlarged enough to serve as an adequate phallus.[21] Otherwise, patients have the option of undergoing metoidioplasty, which involves elongation of the clitoris and use of local and distal flaps to create a neoscrotum and neophallus, preserving erectile and urethral function. Implants and prostheses can be used to help with penile rigidity and appearance of testicular tissue in the scrotum.[23]

Most transgender patients seek surgical sex reassignment as the final step in their transition to their desired sex. Review of the literature reveals that in the past, male-to-female patients reported significant dissatisfaction regarding sensation and their ability to orgasm postoperatively. As techniques have improved in their ability to preserve genital sensation, patients now tend to report significant improvement in quality of life and self-image after recovery from surgery. Two studies have looked at postoperative outcomes and report ability to orgasm and erogenous sensitivity in 65.3% and 93.9% of patients, respectively. Urinary and voiding dysfunction were the most commonly reported symptoms in these studies, with patients reporting urethral stenosis (23%), spraying of urine (20%), and upward urine stream (26%).[25,26] Patients are also at risk for poor wound healing, especially in cases where grafts have been used. This is managed with good patient follow-up postoperatively and careful debridement of granulation tissue when needed. The most important part of surgical management is the preoperative counseling and teaching that is provided to patients. Patients should be counseled thoroughly in the preoperative stage about the need for an adequate recovery period as well as cosmetic

and functional expectations once postoperative healing is complete.

The risk of regret still remains considerable as approximately 1-2% of patients report regret or dissatisfaction.[27] This risk appears to be more common in patients who experience gender dysphoria late in life, and subsequently undergo their transition later.[21] The risk of regret is not trivial, and sex reassignment surgery is an irreversible procedure that can have detrimental consequences if patients are not completely committed to their transition. For this reason, providers evaluating these patients for diagnosis, during the real-life experience, and during hormonal therapy should monitor patients closely for social adaptation and initial improvements in life quality. Similarly, surgeons who perform reassignment surgery should choose their patients carefully and with appropriate scrutiny to try to reduce this risk as much as possible.

As outlined in the 2011 WPATH standards of care, patients must have well-documented gender dysphoria and a mental health professional's referral for breast augmentation, while 12 months of hormonal therapy is recommended. Patients who desire feminizing genital surgery are required to have referrals by 2 separate mental health professionals, 12 months of hormone therapy, and 12 continuous months of living in their desired gender role. Masculinizing procedures such as mastectomy require documented gender dysphoria and a mental health professional's referral while hysterectomy and salpingo-oophorectomy require the same referral as well as 12 months of continuous hormonal therapy. Masculinizing genital surgery has the same requirements as male-to-female vaginoplasty: 2 separate mental health professional referrals and 12 months of continuous hormonal therapy and completion of the real-life experience.

FIGURE 5
Surgical options

Male-to-Female

- Breast/chest surgery: augmentation mammoplasty (implants/lipofilling)
- Genital surgery: penectomy, orchiectomy, vaginoplasty, clitoroplasty, vulvoplasty
- Feminizing procedures: facial feminization surgery, liposuction, lipofilling, voice surgery, thyroid cartilage reduction (tracheal shaving), gluteal augmentation

Female-to-Male

- Breast/chest surgery: subcutaneous mastectomy, chest contouring
- Genital surgery: hysterectomy + salpingooophorectomy, metoidioplasty/phalloplasty +/- implantation of penile/scrotal prostheses, vaginectomy, scrotoplasty
- Virilizing procedures: liposuction, lipofilling, voice surgery, pectoral implants

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Barriers to health care

Similar to the lesbian, gay, and bisexual population, transgender patients have particular medical needs but experience barriers to accessing care. These patients represent a significant underserved population as there has been long-standing marginalization and prejudice against this group of individuals based on their sexual identities or lifestyle choices. As a result, basic needs such as access to education, health care, and housing has been compromised in this group. A national survey study published in 2003 showed that only 30-40% of transgender individuals received routine medical care.[28] The Washington Transgender Needs Assessment Survey conducted from 1998 through 2000 reported on the most common factors contributing to poor access: lack of insurance (64%), inability to pay (46%), provider insensitivity or hostility to transgender individuals (32%), and fear of transgender status revealed (32%).[20] A more recent study looking at 101 male-to-female transgender individuals in New York City showed that 77% of their study participants reported having some form of medical insurance while 81% of participants reported having a general practitioner.[2] While these results are more reassuring than previous survey studies, the percentage of individuals without health care insurance remains greater than the 16.3% of the general population that is uninsured in the United States as of 2010.[29]

Even with health insurance, transgender patients experience obstacles regarding access to health care. The majority of health insurance plans in the United States do not include coverage for most treatments related to gender transition, which imposes a significant financial burden on these patients. Some plans deny coverage for gender-specific care based on a patient's natal sex and only cover care that is consistent with the patient's current gender. Examples include transgender women who develop cancer of the prostate or transgender men who develop ovarian cancer.[30] Some of these problems are due to the coding system that insurance plans use to reimburse care rendered to patients. Some insurance plans simply exclude health care treatments for transpatients even when they are not related to the process of gender transition. The provider plays an important role with these dilemmas and can act as an interface between the patient and the insurance carrier to explain why certain treatments should be covered under the patient's plan.

The following was written in an article published in 2010 in the Journal of Medical Practice Management: "For transgender people, seeing healthcare providers usually involves some degree of 'outing' themselves as transgender, which can be a frightening proposition for members of a community that routinely faces discrimination and stigmatization inside and outside the healthcare

profession."[30] Providers who are knowledgeable about particular transgender health issues and sensitive to the needs of these patients will establish trusting relationships with their patients, which is imperative for providing good medical care. The dynamics of a health care relationship can be very challenging, especially when the patient group is a complex one such as the transgender population. There are, however, practice habits that can be put into effect that might improve patient access to health care. The most important thing that a provider can do is recognize that their personal belief system is mutually exclusive from the medical relationship that is established with any patient.[31] If providers are not comfortable caring for patients who are transgender, a referral list of physicians who provide routine medical care for this community should be easily available to all patients.

Identifying risk factors and screening for them is also an important part of the medical care for these patients. While transgender individuals carry the same risk factors as the general population for most diseases, it is important to recognize that these patients may be very sensitive to screening questions that ask about sexual behaviors and activities. To strengthen the physician-patient relationship and establish trust, providers should explain to patients that their screening questions are routine and that they are posed to all patients regardless of sexual preferences or identity. Additionally, using gender-neutral terminology such as "partner" or "significant other" and asking broad questions such as "Do you have sex with men, women, or both?" allows patients to assume that the provider is both comfortable caring for patients who are lesbian, gay, bisexual, or transgender and knowledgeable about this patient group and their health care needs.[31] It is important to avoid making assumptions about sexual orientation based on an individual's gender identity as there is significant diversity in sexual preference and behaviors among the transgender community. Gender identity does not define one's sexual orientation.

Additional measures can also be taken in the office space to make patients more comfortable with their surroundings. The importance of these measures should be instilled in the entire office staff and cultural competency should be emphasized and taught on a regular basis. Such measures include making a unisex bathroom available for transgender patients,[31] using a transgender individual's preferred name and appropriate pronouns as often as possible, and ensuring that all medical forms and materials are transgender-inclusive.[30]

Health care maintenance

Because of the challenges associated with this highly stigmatized community, there is a lack of data on the actual population size of transgender individuals as well as outcomes after hormonal and surgical therapy. There have been some cases of breast and prostate cancer reported,[16] however in a large series of 2200 patients from 1975 through 2005, no cases of breast cancer were observed.[32] No follow-up studies have followed up patients beyond the age of 65 years; therefore, we cannot determine the actual risk of hormonal therapy on patients beyond this age. Because there is such a paucity of data, there are no published transgender-specific guidelines based on level-1 evidence for the routine health maintenance of these patients. However, preventative health strategies can be extrapolated based on evidence that has been determined to be accurate for the general population. Figures 6 and 7 list the recommended screening guidelines for male-to-female and female-to-male transsexual patients. Before applying these guidelines to patients, one must first keep in mind the patient's natal sex and then take into account the patient's hormonal and surgical status.

For instance, prostate cancer screening is important in male-to-female patients. The prostate becomes atrophic in the setting of androgen suppression, however the risk of cancer remains. For this reason, the Endocrine Society recommends the same screening guidelines for prostate disease recommended for natal men. There are 2 important factors to consider when screening these patients. First, while the preoperative male-to-female transsexual can be evaluated by a standard annual rectal examination after age 50 years, a postoperative patient who has had a neovagina created between the rectum and the prostate may require transvaginal palpation for adequate assessment. Second, prostate-specific antigen (PSA) is sometimes used for prostate cancer screening; however, in the setting of prolonged estrogen exposure, PSA levels can be falsely low.[33] PSA is therefore not an appropriate test for prostate cancer screening in these patients.

The risk of breast cancer is an important consideration in both male-to-female and female-to-male transsexuals. Transwomen sustain long-term exposure to estrogen. Although there has been no conclusive evidence that the risk of breast carcinoma is greater in these patients compared to the general population, risk factors such as longer duration of feminizing hormonal therapy, family history of breast cancer, and obesity should raise concern for providers. There are good data, however, demonstrating the increased risk of breast cancer in postmenopausal women exposed to both estrogens and progestins.[34] Therefore, patients who undergo orchiectomy should be taken off of progesterone soon after surgery, and if therapy is continued, they should be screened earlier for breast cancer. Otherwise, it is reasonable to screen patients according to standard guidelines, which include annual or biennial mammograms starting at age 40 years and then annually after age 50 years. Many of these patients have had breast augmentation, and while routine mammograms are appropriate for screening, providers should acknowledge that in the setting of inadequate screening, magnetic resonance imaging studies are recommended. Most female-to-male patients undergo mastectomy with or without chest-contouring surgery. After this type of surgery, breast tissue still remains and routine screening should be applied to these patients as well, especially if mastectomy only was done.[15] This is because a portion of administered testosterone can be

aromatized to estradiol and some patients may be at risk for estrogen receptor−positive breast carcinoma.

When screening transmen at their annual visits, it is important to know whether or not their pelvic organs (uterus, cervix, ovaries, fallopian tubes) have been removed. If they have not undergone hysterectomy, routine Pap smear guidelines should be followed according to the American Society for Colposcopy and Cervical Pathology (ASCCP). Additionally, abnormal uterine bleeding should be evaluated no differently than in natal women. Prolonged testosterone exposure can lead to an increase in endogenous estrogen levels, which can increase the risk of endometrial hyperplasia and carcinoma[24]; therefore, bleeding in these patients should not be overlooked. As is the case for natal women, there is no recommended screening for endometrial cancer in asymptomatic transmen. Patients who still have their ovaries are at risk for ovarian cancer. While there was concern that exposure to testosterone would increase the risk of ovarian carcinoma in female-to-male patients, there is no evidence to support this.[16] Therefore, these patients are considered to be at similar risk as the general population, and no screening guidelines currently exist. Patients who have undergone total hysterectomy with a history of cervical dysplasia should also have vaginal cuff screening according to the ASCCP guidelines.

Metabolic diseases also need to be considered in transpatients. Androgen suppression and estrogen substitution in male-to-female patients can lead to increases in visceral fat, which is associated with increases in triglyceride levels, insulin resistance, hepatic dysfunction, and elevated blood pressure.[15] While these metabolic changes can increase morbidity in these patients, a study with a median follow-up period of 18 years reported no increase in risk of death from cardiovascular causes in this patient population.[35] Recommendations include using the lowest doses of estrogen available as outlined in Figure 2, with the transdermal route as one of the preferred modes of administration because of its ability to maintain physiologic serum levels of estradiol. Patients should be screened annually for elevated blood pressure, with the following target goals: systolic blood pressure ≤135 mm Hg and diastolic blood pressure ≤80 mm Hg. Per the US Preventative Services Task Force guidelines, if blood pressure remains persistently elevated beyond these parameters, antihypertensive therapy should be initiated. Testosterone therapy in female-to-male patients can lower high-density lipoprotein cholesterol and elevate triglyceride levels, but it is unclear if estrogen therapy has a protective or detrimental effect in male-to-female patients.[36] Based on this information, the recommendation is to monitor lipids routinely. Recommendations for the general population include screening men aged ≥35 years and women aged ≥45 years for lipid disorders (grade A). For patients who have been exposed to prolonged use of testosterone or estrogen, grade-B recommendations should be employed, which include screening for all patients aged ≥20 years. Target goals for low-density lipoprotein levels should be ≤135 mg/dL. Transsexual

FIGURE 6
Metabolic screening recommendations

Cardiovascular disease

General population:

- Men and women should be screened annually for elevated blood pressure after age 18 (A); Target blood pressure is systolic blood pressure ≤135 and diastolic blood pressure ≤80
- Beginning at age 35, men should be tested routinely for lipid disorders (A); men at higher risk for coronary disease should be tested routinely after age 20 (B).
- Beginning at age 45, women should be tested routinely for lipid disorders (A); women at higher risk for coronary disease should be tested routinely after age 20 (B).

Transgender population:

- Screen annually for elevated blood pressure after age 18; Target blood pressure is systolic blood pressure ≤135 and diastolic blood pressure ≤80
- Beginning at age 20, screen routinely for lipid disorders.

Diabetes mellitus

General population: Beginning at age 45, screen every 3 years for diabetes; if symptoms present or blood pressure persistently ≥135/80, screen earlier (B).

Transgender population: Screen annually regardless of age

Osteoporosis

General population:

- Begin screening women every 10 years after age 65 or in younger women whose fracture risk is elevated (B)
- Initiate vitamin D and calcium supplementation after menopause

Transgender population:

- Begin screening transgender women every 10 years after age 65 or in younger women whose fracture risk is elevated or if patients have stopped hormone therapy
- Screen transgender men 10 years after initiation of testosterone therapy and then every 10 years thereafter
- All patients who have undergone gonadectomy should be started on vitamin D and calcium supplementation regardless of age, this is especially important for transgender men on testosterone therapy

Additional screening, transgender population:

Hepatic function: Screen patients annually for liver function abnormalities

Prolactinoma: Measure serum prolactin levels at baseline, at 12 months following initiation of treatment, and biennially thereafter

Adapted from the *U.S. Preventive Task Force (USPTF), American Diabetes Association, Endocrine Society.*

*Grade levels for USPTF recommendations are in parentheses.

FIGURE 7
Cancer screening recommendations

Prostate cancer

General population: Beginning at age 50, men should have a discussion of the risks and benefits of prostate cancer screening. If they desire screening, prostate specific antigen (PSA) +/- rectal examination of the prostate should be done.

Transgender population: Beginning at age 50, transgender women should have a discussion of the risks and benefits of prostate cancer screening. If they desire screening, PSA should not be drawn and instead, rectal or transvaginal examination of the prostate should be done.

Breast cancer

General population: Annual or biennial mammograms are recommended starting at age 40 and then annually after age 50 continuing for as long as a woman is in good health. Clinical breast exam about every 3 years for women in their 20s and 30s and every year for women 40 and over.

Transgender population: Annual or biennial mammograms are recommended starting at age 40 and then annually after age 50 continuing for as long as a woman is in good health. Clinical breast exam annually.

Colon cancer

General population: Beginning at age 50, both men and women should follow one of these testing schedules:

- Flexible sigmoidoscopy every 5 years, or
- Colonoscopy every 10 years, or
- Double-contrast barium enema every 5 years

Transgender population: Same as above; if a transgender woman has a colonic neovagina, she should also undergo vaginoscopy at the time of sigmoidoscopy or colonoscopy; or careful speculum examination

Pelvic organ cancer (ovarian, endometrial, cervical)

- Transgender men who have not undergone hysterectomy should have routine PAP smears as per the *American Society for Colposcopy and Cervical Pathology* (ASCCP) guidelines; transgender men who have undergone hysterectomy but have a history of cervical dysplasia should have vaginal cuff PAP smears as per the ASCCP guidelines.
- Transgender women do not require routine PAP smears. The neovagina should be examined routinely for presence of HPV condyloma.
- There are no guidelines for screening asymptomatic patients for endometrial or ovarian cancer; transgender men should have a bimanual pelvic exam every 1-2 years and a pelvic ultrasound if symptoms are present.[a]

HPV, human papillomavirus; *PAP*, Papanicolaou.

[a]If transgender men have undergone hysterectomy and oophorectomy, a discussion between the provider and patient is recommended to assess the risks and benefits of performing routine pelvic exam.

Adapted from the *American Cancer Society, U.S. Preventive Services Task Force, American Congress of Obstetrics and Gynecology.*

patients who are maintained on hormones should also undergo annual testing for diabetes with fasting glucose levels, glucose tolerance testing, or hemoglobin A1c levels. Patients on estrogen maintenance are at especially high risk for developing insulin insensitivity but patients on testosterone therapy are at risk as well and should be tested routinely. Estrogen and testosterone therapy can also cause a transaminitis that is usually self-resolving. In patients undergoing routine lipid and glucose screening, an initial evaluation of liver function should be done and repeated at routine annual visits or sooner if the patient develops symptoms suggesting hepatic disease.[15]

Patients who choose to have sex reassignment surgery often undergo gonadectomy, and hormonal therapy should be altered after removal of either the ovaries or testes. Progesterone or androgen-suppressing therapy can be stopped in all transsexual patients, while estrogen and androgen therapies must be continued to avoid loss of bone mineral density and the development of osteoporosis. Vitamin-D and calcium supplementation should be initiated according to standard guidelines for the general population. Transmen who have been on testosterone therapy for a prolonged amount of time may require bone mineral analysis via dual energy X-ray absorptiometry (DEXA) scan earlier than the recommended age as it is unclear what effects exogenous testosterone may have on bone loss. Vitamin-D and calcium supplementation can then be started according to DEXA results in this population. The Endocrine Society currently recommends that bone mineral density measurements should be obtained if risk factors for osteoporosis exist, especially in patients who have stopped sex hormone therapy after gonadectomy.[15]

The incidence of venous thromboembolism (VTE) among male-to-female transgender persons on estrogen therapy ranges from 0.4-2.6% per year.[16,17] The highest risk of VTE is among patients who are maintained on high doses of synthetic estrogen, namely ethinyl estradiol. Patients who are taking this hormonal therapy should be tapered off and transitioned to a lower-dose estrogen regimen, preferably via a transdermal route. There is no recommended screening for VTE, but index of suspicion should be raised in patients who present with extremity edema or pain or pulmonary symptoms concerning for pulmonary embolus, especially if they are age >40 years, are obese, have decreased mobility, smoke, or have a personal or family history of thrombophilia.

Data from the Centers for Disease Control and Prevention (CDC)-funded human immunodeficiency virus (HIV) testing programs show a high rate of new HIV diagnoses in the transgender community. In 2009, the CDC reported that the prevalence rate for newly identified HIV infections was 2.6% among transgender individuals compared to 0.9% for natal males and 0.3% for natal females. Notably, 52% of these diagnoses were made in the nonclinical setting.[37] A metaanalysis reviewing 29 publications showed that 11.8% of transgender women reported a diagnosis of HIV, but when tested, the HIV rate was 27.7% (range, 16−68%). Additionally, 73% of male-to-female transsexuals who tested positive for HIV were unaware of their status.[38] Given these data, providers must make a point to identify risk factors for HIV that may be more prevalent in this population than in others. Among newly diagnosed transgender women,

50% of them report substance abuse, commercial sex work, incarceration, homelessness, and/or sexual abuse.[37] Discrimination may explain why some transgender individuals experience economic hardships and, as a result, engage in high-risk behaviors such as commercial sex work. Preoperative transgender women are more likely to engage in this behavior,[39] subjecting them to high-risk receptive intercourse, which increases their risk for HIV infection. Additionally, social stigma and poor self-image may also play a role in risky behaviors involving unprotected receptive intercourse, as these individuals seek acceptance and gender affirmation and fear rejection by their sex partners. Patients who participate in high-risk behaviors such as unprotected sex with different partners, anal intercourse, needle sharing for injection of hormones or illicit drugs, or who have a history of sexually transmitted infections should be screened routinely (every 6-12 months) for blood-borne diseases which include HIV and hepatitis B and C. Additionally, patients should be screened for other infections including syphilis, gonorrhea, and chlamydia. In male-to-female transsexuals, cultures of the urethral meatus are acceptable for gonorrhea and chlamydia testing. For patients who do not engage in risky behaviors, 1-time testing is indicated followed by as-needed testing throughout their lifetime.

The role of the gynecologist

According to Healthy People 2020, a major governmental health care goal is to improve the health, safety, and well-being of the lesbian, gay, bisexual, and transgender population.[40] Gynecologists play an important role in reaching this goal, as transpatients often seek primary care in gynecologic practices. Male-to-female transsexuals sometimes prefer to see a gynecologist for their annual health care as this helps them to affirm their gender and also gives them the opportunity to share any gynecologic concerns such as recurrent neovaginal and urinary tract infections, problems with voiding, and pain with intercourse. Neovaginal prolapse as well as anatomic urinary tract dysfunction, while rare, does exist.[41] Patients may initially seek the care of a gynecologist to address the problem and to determine the need for referral to a subspecialist. Additionally, some patients prefer to have their annual breast examination with a gynecologist. Transgender men sometimes seek gynecologic care as many of these patients do not fully transition with sex reassignment and do not have their pelvic organs removed and need routine screening such as Pap smears and bimanual pelvic examinations. In addition, some patients may receive their hormonal treatments and surveillance through reproductive endocrinology specialists who may prefer to refer patients to gynecologists in their practice for routine health management to facilitate good continuity of care.

For all the reasons above, gynecologists need to be familiar with the health care needs of these patients. Care should be rendered according to standard guidelines based on level-1 evidence for the general population, but then some alterations should be made with important considerations in mind including biological sex, surgical status, declared gender, and past or current use of hormonal therapy. Additionally, gynecologists should be aware of the most commonly used hormonal therapies, which ones are given preoperatively and then postoperatively, and how they can be changed if there are metabolic concerns. Although trained endocrinologists usually make adjustments to regimens, providers caring for these patients should have general knowledge to help guide their management in other aspects of their care.

Gynecologists may play an important role in counseling patients about fertility or referring them to reproductive endocrinologists for care. The initial discussion may take place in the gynecologist's office. Feminizing and virilizing hormonal regimens have been shown to diminish fertility in patients.[42] The significant challenge is that these discussions should take place prior to the initiation of hormonal therapy. If patients disclose that they are transgender during a routine office visit, they may require counseling regarding their transition options. During that initial discussion, options about fertility can also be addressed. Although there are no data on the rates of infertility among transsexual patients treated with hormones, data can be extrapolated from patients who have experienced damage to their gonads as a result of cancer treatments.[14] Male-to-female patients should be given the option of sperm preservation in sperm banks prior to initiating hormones. If patients have already initiated hormones, there are data that report eventual recuperation of sperm count after a hormone-free period[43] and so, these patients can be given the option to stop hormonal therapy temporarily to bank their sperm. There are also limited data on female-to-male preservation of fertility. These patients can consider oocyte or embryo cryopreservation prior to starting therapy, while those who have already initiated hormones have the option of interrupting their treatment to undergo ovarian stimulation with subsequent oocyte retrieval and freezing. Studies have shown that there has been some success in ovarian recovery after cessation of testosterone with subsequent successful pregnancies.[44,45]

Lastly, gynecologists should be aware of the barriers that transpatients face with regards to accessing care as well as feeling comfortable once they have found a provider. Simple things can be done within the office setting to ensure that patients understand that they are in a safe space and that they will receive the same care as other patients. Most importantly, they should feel safe disclosing their gender identity as well as their sex preferences so that the provider may take care of them and identify all possible risk factors for disease. This can be accomplished with an open-minded approach to patient care, use of screening questions that do not discriminate against any individual or group, and demonstration of knowledge of the general principles of transgender health. ■

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