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Feature: Transgenderism

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Transgendered individuals are people who, by all known biologic measures, are male or female, yet feel like a member of the opposite sex. The discomfort they suffer is called gender dysphoria. Theirs is a relatively rare condition and cannot be explained by factors such as chromosomes, prenatal hormones or toxin exposure, genital variability, postnatal circulating hormone levels, gender of rearing, birth order, or the presence or absence of same-sex siblings.

Is it possible that the brains of the transgendered are uniquely "wired"? Subtle differences between female and male brains have been reported for decades in research studies that identify gender-related size differences between specific brain nuclei by staining slices of post-mortem specimens.¹ One recent study showed that the nuclei of transgendered male-to-females (MTFs) are the size of the nuclei of genetic females.² An earlier study revealed that males dying of prostate cancer who had been treated for years with female hormones, and females dying of virilizing adrenal tumors, had nuclei consistent with their genetic sex.³ Their hormonal exposure did not affect the gender-specific nuclei of their brains.

Gender dysphoria is listed as a psychiatric condition in the psychiatric diagnostic coding manual DSM-IV. I believe that the psychiatric manifestations are a reaction to the situation, not the underlying condition. A transgendered individual who has not had hormonal therapy or surgery may require psychopharmacologic medications, but after a patient receives medical and/or surgical treatment, psychotropic medicines are often unnecessary.

Nearly all transgendered adults recall feelings of being in the wrong body early in childhood. Patient histories resonate with the common theme of dressing secretly in the clothes of the opposite gender during childhood. However, the age at which a transgendered individual fully acknowledges his or her gender identity varies from mid-childhood to middle age. Delayed acknowledgment can usually be traced to a fear of stigmatization and rejection by family, friends and employers.

The majority of children who express recurrent interest in being the opposite sex are not transgendered, although many become homosexual.⁴ A small percentage of children who are emphatic and consistent

in their desire to be the opposite gender (less than 20% of the above) prefer to be called by a pronoun and name consistent with their gender identity. Their friends, dress and activities correspond with that identity. Their greatest fear is puberty because of the irreversible changes that threaten how they are perceived (their "gender attribution"). During adolescence, when unwanted and permanent secondary sexual characteristics transform the patient's body into an adult form that is asynchronous with the brain, depression and anxiety are typical reactions. When menses become a monthly reminder of femaleness in a teenager with a male identity, self-abusive behavior is common. The incidence of suicide among transgendered youth is high. ⁵ Adult transgendered individuals who find it threatening to acknowledge their gender identity publicly may adopt a lifestyle of marriage and parenthood that matches their genetic sex. Inevitably, maintaining this charade takes its psychic toll.

Who is qualified to assess a patient's condition for referral for endocrine treatment and ultimate surgery? "Standards of care" have been created by the Harry Benjamin International Gender Dysphoria Association, a professional society that includes mental health professionals, endocrinologists, internists and surgeons (<http://www.hbigda.org>). The standards define stages of treatment, beginning with "extensive exploration of psychological, family and social issues" by a mental health professional who has abundant experience working with this population, and only then moving to physical intervention, which should take place in stages, from reversible to irreversible interventions.

Physicians may be uncertain how to address transgendered patients who have not legally changed their name and gender but have transitioned to a gender role consistent with their gender identity. Some states require reconstructive surgery - genitoplasty or mastectomy - before allowing name and gender changes on documents such as driver's licenses and health insurance cards. Whether or not patients have made legal changes or undergone surgery, they are entitled to the dignity of being referred to by the name and pronoun of choice. Male-to-female patients should be offered a gown in the exam room, and female-to-male (FTM) patients should be asked what they prefer to wear during the exam. No assumption should be made about the patient's sexual orientation. Like anyone else, a transgendered individual may be straight, gay or bisexual. Sexual orientation reflects physical attraction, not gender identity.

The labeling of transgenderism as a psychiatric condition has the ironic effect of inducing psychological problems in transgendered individuals. This fuels the notion that a psychiatric disorder is at the heart of the condition, which influences the diagnostic coding and billing structure. Under the DSM-IV code, few health insurers in the United States cover the cost of hormonal replacement therapy. Mastectomies in FTMs, which cost \$6,000 to \$10,000, and genitoplasties (sex reconstructive surgery) in MTFs, which cost \$15,000 to \$25,000, are considered by almost all health insurers to be cosmetic surgeries on patients with a mental illness.

To enable patients to transition physically, endogenous gonadal sex steroid output must be lowered to levels consistent with the gender of choice, which may not be easy. Both MTFs and FTMs require supraphysiologic doses of "crosshormones": estrogen for MTFs, testosterone for FTMs. High dose estrogen poses a risk of blood clots, which can be fatal if they travel to the lungs (pulmonary embolism) and doses of testosterone sufficient to prevent menses can induce hypertension, cystic acne and excess red blood cell production with the risk of blood flow "sludging." Alternatively, endogenous sex steroids can easily be suppressed by GnRH analogues, which block pituitary gonadotrophin (LH and FSH) release,

enabling cross-hormone treatment to be accomplished with safer physiologic doses of estrogen or testosterone. Unfortunately, GnRH analogues are prohibitively expensive in the US, and patients are forced to take the higher doses of sex steroids until they have their gonads removed. Genitoplasty in MTFs and reduction mammoplasty in FTMs are not covered by most health insurers, and patients may have to wait years saving for it.

In the Netherlands and Belgium, national health insurance covers all costs related to evaluation and treatment of transgendered individuals, including children. [6](#) Interdisciplinary gender teams evaluate patients psychologically, and patients become potential candidates for sex reconstructive surgery at government expense after living for at least a year in the gender of choice (the "real-life experience") while taking corresponding sex steroid hormones. This discrepancy in coverage across nations raises questions about US health insurance policy decisions.

Because treatment with cross-gender hormones has irreversible effects, challenging choices inevitably arise. For the MTF, estrogen produces breast enlargement and diminished sperm production. Some MTFs request sperm banking before estrogen treatment or gonadectomy just to maintain their reproductive capacity, regardless of who will receive that sperm. For the FTM, testosterone produces a deeper voice, facial hair, temporal balding. Loss of ovulation and menses ensue, and the ovaries become polycystic while retaining retrievable ova. When cryopreservation of ova becomes technically routine and successful, some FTMs will request the procedure to serve as egg donors for their partner or surrogate.

A significant ethical question in transgender care concerns potential intervention with children. Should transgendered children who have had a careful and protracted evaluation by a skilled gender specialist be compelled to complete puberty before being offered the same therapy used for adults? No national or international protocol exists, and there are opposing views on how to proceed. One side argues that physical intervention should be delayed until the completion of puberty because teenagers are more likely than adults to change their minds about their gender identity. The opposing view, with which I concur, argues for early endocrinologic intervention to prevent the severe depression that accompanies the onset of an unwanted puberty and to avoid the physically and psychologically painful procedures required to reverse puberty's physical manifestations.

A model protocol currently employed in the Netherlands begins with a lengthy screening process in gender-variant pubescent teens at the "Tanner 2" stage of pubertal development: breast budding in girls and testicular volumes of 8 cc, preceding phallic enlargement in boys. At this stage the pubertal manifestations are reversible. GnRH analogues are given for at least two years, potentially until age 16, when adolescents in the Netherlands are capable of giving informed consent to receive crosshormones. By blocking puberty, GnRH treatment buys time for FTMs to achieve a height more typical of males and for continued assessment of all patients' desire to transition. If the Dutch clinical trial proves medically and psychologically safe, it will become the standard of care in the Netherlands, and treatment will be covered by the government health insurance.

Adoption of such therapy in the US, except by a research protocol, is unlikely to be reimbursed by most health insurers as long as transgenderism continues to be coded and billed as a psychiatric condition. The only alternative drug capable of achieving comparable gonadotrophic suppression is high

dose progesterone, which has effects similar to high dose prednisone or cortisone and can produce ACTH suppression, fluid retention, "moon face," central obesity and insulin resistance.

"Precocious puberty" is the only approved indication for pediatric use of GnRH analogue therapy in the US. For a patient's insurance to pay for this drug a physician would have to use this diagnosis for an 11-year-old FTM or 12-year-old MTF, even though the patient hardly meets the age criteria of sexual precocity. If the Dutch protocol is approved by the Harry Benjamin Society, would it be right for US health insurers to withhold payment for GnRH in properly screened transgendered teens?

Transgendered individuals have long faced discrimination in medical institutions, including physicians' offices and hospitals. [7](#) Reminiscent of the medical/psychiatric approach to homosexuality not so long ago, some physicians and psychologists maintain that the goal of psychiatric treatment is to convince transgendered individuals to remain in the gender role of their genetic sex, which is an impossibility for most patients. Everyone involved in patient care should have some awareness of gender identity disorders, however rare they may be. Primary care physicians interested in providing hormonal replacement therapy for transgendered patients should consult the Harry Benjamin Society Standards of Care. Physicians and mental health professionals who are neither comfortable nor sufficiently knowledgeable to treat transgendered patients should refer them to more experienced colleagues.

Footnotes

1 Woodson JC and Gorski RA. Structural differences in the mammalian brain: reconsidering the male/female dichotomy. In Matsumoto A (ed.) *Sexual Differentiation of the Brain*, New York and London: CRC Press, 2000.

2 Kruijver FP et al. Male-to-female transsexuals have female neuron numbers in a limbic nucleus. *J Clinical Endocrinology & Metabolism*. 85(5):2034-41, 2005.

3 Zhou JN et al. A sex difference in the human brain and its relation to transsexuality. *Nature*. 378(6552):15-16, 1995.

4 Zucker KJ and Bradley SJ. *Gender Identity Disorder and Psychosexual Problems in Children and Adolescents*, New York and London: The Guilford Press, 1995

5 Kreiss JL and Patterson DL. Psychological issues in primary care of lesbian, gay, bisexual, and transgendered youth. *Journal of Pediatric Health Care*. 11(6):266-74, 1997

6 Cohen-Kettenis PT and Pfafflin F. *Transgenderism and intersexuality in childhood and adolescence. Making choices*, Thousand Oaks and London: Sage Publications, 2003

7 Feinberg L. *Transgender warriors*, Boston: Beacon Press, 1996 Additional readings Boylan JF. *She's not there*. New York: Broadway, 2003

Additional Reading

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