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How Should Physicians Help Gender-Transitioning Adolescents Consider Potential Iatrogenic Harms of Hormone Therapy?

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Abstract
Counseling and treatment of transgender youth can be challenging for mental health practitioners, as increased availability of gender-affirming treatments in recent years raises ethical and clinical questions. Is a gender identity diagnosis helpful? What is the right time to treat, and should the adolescent's age matter in decision making? In this article, we discuss these questions in light of a case in which an adolescent wishes to pursue hormone therapy. Our analysis focuses on the importance of balanced decision making when counseling and treating adolescents with nonconforming gender identities. We argue that clinicians' communicating appropriate expectations about the effectiveness and limitations of hormone therapy and the risks of psychological and physical iatrogenic effects is critical.

Case

Dr. Giles first met Jackie about a month ago when her father, Mr. Jensen, brought her to his endocrine clinic. Jackie was 12 and just starting to hit puberty, but she resented the changes that were happening to her body. She had lived the last year as "Jack," wearing "boy" clothes and keeping her hair short. "Jackie has shown tendencies toward traditionally male interests since childhood," her father explained. "She would take on male roles when playing make-believe and would prefer playing with the boys in her class."

As Jackie grew, however, she was not satisfied with being a girl who did "boy" things anymore. "I want to be a boy," she told her parents. The Jensens did not want their child to have to play make-believe for the rest of her life. They had heard about transgender children before, and after reading more about the subject, they came to believe that their daughter was transgender. When Jackie began going through puberty, things got difficult. The victim of bullying, she suffered emotionally. Her usual bright personality became subdued, and she struggled in school. Worried, the Jensens took Jackie to a therapist, but it didn't seem to help. A psychiatrist diagnosed Jackie with gender

dysphoria (GD), characterized by distress about the mismatch between gender identity and biological sex. As things escalated, they decided to seek out a more permanent solution, which brought them to Dr. Giles's door.

"We are interested in hormone therapy to prevent puberty and help Jackie look more like a boy," they explained, pamphlet in hand. Dr. Giles was apprehensive about starting hormone therapy in someone so young. He was aware that many children with GD outgrow the condition; additionally, he took issue with the classification of GD in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders*. He worried that framing nonconforming gender identity experiences as a pathology contributed to the psychological distress many transgender people feel and influenced their desire for gender-affirming therapy.

He also worried about long-term risks and side effects that come with hormone therapy and whether Jackie could understand at her age how these consequences would affect her over time. Jackie would most likely undergo puberty suppression, giving her more time to explore her feelings regarding her gender. Dr. Giles was concerned that this therapy could stunt her growth and lead to weight gain and fertility issues and could also cause her to experience menopause-type symptoms and possibly depression. If Jackie underwent androgen therapy for gender transition, she could even be at risk for developing insulin sensitivity, hyperlipidemia, and an increased hematocrit, compromising her metabolic health.

On the other hand, according to Jackie and her family, not going through with the treatment could cause Jackie significant psychological harm. Dr. Giles was now faced with the difficult decision of determining whether Jackie's experience of gender identity-related suffering justified accepting the iatrogenic risks associated with treating it.

Commentary

The problems experienced by Jack and the considerations with which Dr. Giles is confronted are a representative reflection of the challenges in transgender care. Growing up with gender dysphoria (GD) can be problematic for several reasons for the transgender teen. In puberty, the development of the body in an undesired direction is generally distressful. Being a victim of bullying and stigmatization as a consequence of rigid and stereotyped gender norms can have a strong negative effect on the psychological health and quality of life of an adolescent with GD [1]. And, in addition, interventions that can be provided by a (mental) health professional to reduce GD (e.g., hormone therapy) are generally efficient but may have iatrogenic side effects. Decisions about the diagnosis and gender-affirming treatment of gender nonconforming youth should therefore always involve weighing the potential benefits and harms for a given individual in a given situation, society, or culture. In light of the available guidelines and the scientific literature, we will discuss three important issues that are closely related to

those that Dr. Giles is confronted with: whether a diagnosis is helpful, how to determine whether hormone therapy should be offered, and whether and how the adolescent's age should matter in decisions about how to treat gender identity problems.

To Diagnose or Not to Diagnose?

In the two most widely used classification systems of (mental) diseases—*the International Statistical Classification of Diseases and Related Health Problems* (*ICD*) and the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*)—a separate gender identity diagnosis was not described until the publication of *ICD*-9 in 1975 and *DSM*-III in 1980 [2]. In the *DSM,* transsexualism was later changed to "gender identity disorder" (*DSM*-IV) and "gender dysphoria" (*DSM*-5) [2]. In the process of revising the *DSM*-IV (now the *DSM*-5) [3, 4] and in updating the *ICD*-10 (into the *ICD*-11), the gender identity diagnoses generated several controversies, including the discussion of the need for a diagnosis per se [5, 6]. A central topic in these discussions is that diagnosing people as having a mental disorder can be pathologizing and stigmatizing [7, 8]. At the same time, having a diagnosis is, in many health care systems around the world, a requirement to access care, including gender-affirming medical treatment [9]. The possible stigmatizing and pathologizing effects of a gender identity-related diagnosis (e.g., increased chance of discrimination, social exclusion) should thereby be weighed against the drawbacks of *not* diagnosing with regard to the inability to receive specialized and possibly reimbursed care, support and advice, and legal protection or a protected status. It is thereby advisable that this harm-benefit analysis not be an individual undertaking by the (mental) health practitioner but rather be a joint process wherein clients (and in the case of minors, their families) are involved. In addition, it is important to keep in mind that the outcome of this analysis can vary widely among different individuals.

To Treat or Not to Treat?

A central question in the counseling of children and adolescents with GD is: What is the right time to treat?

Prepubertal children. With regard to prepubertal children, the *Standards of Care* (*SOC*) of the World Professional Association for Transgender Health is clear in that no medical interventions should be provided before the onset of puberty [10]. The primary reason for this recommendation is that GD in childhood does not always persist into adolescence or adulthood. A review focusing on the development of children with GD showed that the gender nonconforming children in the studies were likely to identify as lesbian, gay, or bisexual adolescents or adults at the time of follow-up and that the GD had remitted around or after puberty for the majority of the children (85.2 percent) [11]. In addition, the ability to predict whether gender nonconformity in a child will persist or desist in the future is limited [12-15]. Therefore, it is generally seen as strongly inadvisable to intervene medically in this period [11].

In consequence, the role of a mental health professional should be supportive and focused on helping the child and the parents to deal with the uncertainty of a future outcome (i.e., whether the GD will persist or not) and possible gender-related problems (e.g., stigma) or nongender-related problems (e.g., coexisting depression or anxiety) and on exploring the child's feelings as he or she continues to develop. For most adolescents with GD, the experience of their body's development in puberty, their changing social position, and their first explorations of love and sexuality provide valuable information about their feelings of GD, leading to the intensification of GD in some and the remittance of GD in others [16].

Adolescence. In the event that GD persists into adolescence, medical interventions (i.e., hormone therapy) are a realistic option for treatment. However, whether to introduce hormone therapy is not a one-time decision after a diagnosis of GD but rather a gradual decision process within a multidisciplinary stepwise treatment approach. The approach is multidisciplinary in the sense that the mental health professionals (e.g., psychologist, psychiatrist) and medical health professionals (e.g., pediatric endocrinologist, pediatrician) work closely together in counseling the client; stepwise treatment always first starts with a psychological assessment without medical interventions, after which fully reversible interventions (i.e., puberty suppression) may be provided, followed by partially reversible interventions (i.e., cross-sex hormones) and irreversible interventions (i.e., gender-affirming surgery) [17].

In the first (psychological) diagnostic phase, the nature and characteristics of the adolescent's gender identity and psychosocial functioning are explored. Treatment to suppress puberty can be initiated if: (1) the criteria for a GD diagnosis are met; (2) puberty has started (Tanner stage 2-3); (3) the adolescent has demonstrated long-lasting and intense GD; (4) the GD feelings intensified with the onset of puberty; (5) coexisting medical, psychological, or social problems have been addressed; and (6) both the adolescent and parents have consented (if the adolescent has not reached the age of medical consent) [10]. Puberty suppression using gonadotropin-releasing hormone analogues (GnRHa) prevents the development of undesired secondary sex characteristics (i.e., feminization in birth-assigned girls and masculinization in birth-assigned boys), allowing adolescents to further explore their GD without the distress of a further-developing body and possibly preventing "risky" (unnecessary) surgical interventions when the patient reaches the age of medical consent [18].

Before this extended diagnostic phase with the use of puberty suppression is started, it is of great importance that both the mental and medical health professional communicate appropriate expectations about the effectiveness and limitations of hormone therapy and the risks of psychological and physical iatrogenic effects of hormone therapy as well as possible future gender-affirming interventions [19]. Although puberty suppression has a positive effect on psychological functioning for

many adolescents [20] and is fully reversible (since puberty reinitiates when treatment is stopped), and although adverse events have not been reported in evaluation studies [21-23], iatrogenic risks have to be taken into account. It has been shown that GnRHa treatment influences bone mass development in delaying peak bone mass accrual [23] and that it may cause hypertension (especially in birth-assigned girls) [24]. Adolescents are therefore advised to maintain a healthy lifestyle through appropriate weight maintenance, sufficient weight-bearing exercise, and adequate calcium and vitamin D intake [25]. In addition, from our clinical experience, most adolescents and parents experience puberty suppression as the first step in gender transitioning. It is therefore important to discuss the iatrogenic risks of possible future gender-affirming treatments (e.g., cross-sex hormones and gender-affirming surgeries), although it may be several years before the adolescent is eligible for such treatments. Such discussions might, for instance, include informing patients about genital sensitivity after genital surgery and about the possibility (in case of hormonal therapy) or certainty (in case of removal of the uterus and ovaries) of fertility loss [26].

Whether certain treatment interventions are offered to adolescents with GD is not the mental health professional's decision of what is in the best interest of the adolescents but rather a decision in which the adolescents are involved [10]. The role of the (mental) health professional is thereby to evaluate whether an adolescent fulfills the criteria for treatment according to the *SOC* [10] and inform the patient (and parents) about treatment effectiveness and safety, taking into account the degree of the individual adolescent's psychosocial functioning and social support. The adolescent (and parents) may then decide, based on the provided information about a treatment's potential risks and limitations, whether to start with a certain treatment or not.

What about Age?

After the introduction of puberty-suppressing treatment for adolescents with GD in 2000 in the Netherlands [27], the availability of the treatment has gradually increased, and it is now offered in several parts of the world [21, 28, 29]. In contrast to the early days, treatment procedures nowadays generally do not use age as a criterion to intervene with puberty suppression or to start hormone therapy [28, 30]. The current *SOC* guidelines do not set strict age criteria for the start of either intervention [10]. This is somewhat remarkable since the only scientific evidence of the psychological efficacy [20, 31] and medical efficacy and safety [21-24, 32] of the treatment is based on the "Dutch protocol" as it was introduced. At that time, the protocol set strict minimum age criteria for starting puberty suppression (12 years of age), cross-sex hormone treatment (16 years of age), and gender-affirming surgeries (18 years of age) [33].

Although the evaluation of the different treatment protocols contributes to knowledge of the safety of using puberty suppression and hormone therapy in transgender youth, from a clinical perspective, it seems reasonable that the age of adolescents with GD

should not be the primary focus. The decision of whether puberty suppression or hormone therapy is offered should be based on not only the aforementioned criteria of bodily development, degree of GD, and psychological suffering and stability but also the degree to which the adolescent is able to oversee the consequences of certain treatments and make a well-informed decision. The extent of the adolescent's "psychological maturation," although often a natural derivative of age, may well differ among adolescents. Therefore, "psychological maturation" seems to be a more valid criterion for transgender youths' eligibility for treatment than a strict age criterion.

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