# Management of transgender and gender-diverse children and adolescents

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## INTRODUCTION

Children generally are designated a gender at birth based upon genital anatomy or chromosomes. For most children, gender designation correlates with gender identity, which is the innate sense of maleness or femaleness. However, some children have a gender identity that does not correlate with designated gender. These children are called transgender or gender-diverse (TGD) youth ( table 1). (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Terminology'.)

The trajectory of gender diversity in childhood is unpredictable; some children with gender diversity will grow up to be transgender adults, and some will grow up to be cisgender adults (ie, adults in whom gender identity matches genital anatomy). (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Trajectory'.)

This topic will provide an overview of the management of gender diversity in children and adolescents. Gender development and the clinical presentation of gender diversity in children and adolescents are discussed separately. (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Referral'.)

## OVERVIEW

Evidence to guide the management of gender diversity in children and adolescents has increased with the increasing numbers of multidisciplinary centers providing treatment for

TGD youth [1-10]. This information supplements the experience from case series of adults who underwent gender-affirming surgery [11].

In the absence of a clear understanding of the etiology of gender diversity, a variety of views influence the management approach and may be applied according to the individual patient's needs and goals. Patient-centered approaches to treating TGD children and adolescents have been outlined by the American Academy Pediatrics [12], University of California, San Francisco Center of Excellence for Transgender Care [13], the Endocrine Society [14], the American Academy of Child and Adolescent Psychiatry [15], and the World Professional Association for Transgender Health [16,17]. Our approach is generally consistent with the recommendations in these guidelines.

The information provided in this topic review is intended to allow primary care providers to educate and support patients and families of TGD youth and to coordinate care, provide referrals, provide additional psychosocial support from the medical home, and monitor patients receiving care from specialists (eg, monitoring laboratory work, drug side effects, drug-drug interactions).

## GUIDING PRINCIPLES

Several principles guide the treatment of TGD youth; these include [5,6,15,18-21]:

- The safety and well-being of the youth and their family members is foremost. Family acceptance and other affirming environments that create space for youth to express and grow into their authentic self are critical for healthy development [22-24]. Other treatment decisions must consider the potential for decreased sense of self-worth, depression, self-harm, suicidality, verbal victimization, physical victimization, etc. (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Associated concerns'.)

- Care for TGD youth is determined according to the individual's gender development, needs, and goals. Given the spectrum and fluidity of gender identity, it is important for health care providers to elicit and understand the specific needs of individual patients [25]. The degree and type of mental health and medical support and interventions may vary. Not all TGD youth desire phenotypic transition, hormones, or surgeries.

- Clinicians who are neither comfortable nor willing to become sufficiently knowledgeable to treat TGD patients should refer them to more experienced colleagues. Understanding that TGD persons are increasingly visible and continue to seek out both medical and psychosocial resources, providers have increasing responsibilities to be both inclusive and have some knowledge of issues relevant to

TGD patients. (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Epidemiology'.)

## TYPES OF INTERVENTIONS

### Mental health interventions

**Mental health approaches** — There are several mental health approaches to support TGD children and adolescents explore their gender identity and find a gender role that is comfortable [16,26]. Treatment options may be influenced by family expectations, cultural differences, opinions of health professionals, insurance coverage, and availability of services.

The specific approach for a given child or adolescent is individualized. The process may or may not involve recommendations for a change in gender expression or body modification; what helps to alleviate gender dysphoria in one person may be very different from what helps to alleviate it in another.

- **Preferred approach** – Affirming approaches are preferred; they are recommended by many professional organizations. (See 'Society guideline links' below.)

  - **Affirming** – Affirming approaches focus on gender identity/body congruence and actively promote exploration of gender development and self-definition within a safe setting [12,18,27,28]. A fundamental concept of this approach is that gender diversity is not a mental illness. It is inappropriate to pathologize the child or adolescent's behaviors or to assign a diagnosis. With the help of affirming psychotherapy, some individuals can integrate their gender-diverse feelings into the gender they were designated at birth; others may be able to alleviate their gender dysphoria through changes in gender role and expression [16,29]. (See 'Social transition' below.)

    The authors of this topic review support affirming approaches – from medical and mental health professionals, as well as parents/caregivers – for TGD youth. The growing medical evidence supports careful listening, thoughtful discussions, and patient-centered approaches to gender exploration.

- **Approaches that are not recommended** – Approaches that are not recommended and potentially harmful include wait-and-see approaches, redirection, and reparative therapy [12].

  - **Wait-and-see** – The wait-and-see approach (also called watchful waiting) involves waiting to see if the child's gender identity will change as the child gets older [18]. Caregivers who take this approach may allow cross-gender play and clothing within

the home or support both masculine and feminine activities as the child explores their interests in other social settings. The wait-and-see approach assumes that gender is binary and becomes fixed at a certain age; it pathologizes gender diversity and fluidity [12]. It is distinguished from following the child's lead, an affirming approach that allows the child to present in the gender role that feels correct and moves at a pace determined by the child. (See 'General suggestions' below.)

- **Redirection** – Some mental health therapists encourage caregivers to use positive reinforcement to try to "redirect" children toward behavior that is more typical of their birth-designated sex or less gender specific. The goal of redirection is to eliminate gender-diverse desires and expressions over time [30]. This approach is not recommended because negative reinforcement (eg, shaming the child for gender-diverse expression) has substantial negative mental and social health consequences.

- **Reparative therapy** – Reparative therapy (also called conversion therapy) claims to be able to "cure" a transgender identity. It is still practiced in certain religious and conservative communities. This approach was initially used in the 1970s [31,32]. Reparative therapy is considered **unhelpful and potentially harmful** by most professional organizations, including the American Academy of Child and Adolescent Psychiatry, the American Academy of Pediatrics, the World Professional Association for Transgender Health, the Society for Adolescent Health and Medicine, and the Substance Abuse and Mental Health Services Administration [12,15,16,33-37]. In the United States, several states, counties, and cities ban reparative therapy. The Movement Advancement Project provides a map of localities that ban reparative therapy.

**Indications for mental health referral** — Referral to a mental health provider may be warranted for [28,38]:

- Prepubertal children with evidence of gender dysphoria (eg, aversion to aspects of their body associated with sex; wish to live as opposite sex); coexisting anxiety, depression, or suicidality; or serious interpersonal conflicts with peers (eg, bullying) or parents. Bullying that occurs at school should also be addressed by school personnel.

- Any youth who wants additional support and resources to explore transgender and/or nonbinary gender identities.

- Peripubertal and postpubertal youth who are not gender dysphoric but seeking additional psychosocial support and planning for affirmation ( table 2).

- Parents of TGD children and adolescents who are uncomfortable or rejecting of their child's identity and behaviors.

  (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Referral'.)

**Phenotypic interventions**

**Social transition** — "Social transition" is a reversible intervention in which the youth lives partially or completely in the preferred gender role by adapting hairstyle, clothing, pronouns, and possibly assuming a new name. Social transition also may include wearing make-up or clothing modification to hide the effects of puberty (eg, wearing a binder to hide breast development, tucking the penis and testicles so they are not visible, wearing protheses or packers to simulate body parts), and using devices that permit urination while standing (for affirmed males).

Patients and families may decide to have a "trial run" to allow the child to see how it feels and the parents and health care providers to see how the child responds. Patients and families decide in advance the extent of the changes (eg, clothing, pronouns, name), whether and to whom to disclose, and how to handle common potential challenges (eg, bathrooms, locker rooms, sleepovers).

Decisions regarding social transition are made on a patient-by-patient basis after considering the potential benefits (eg, alleviation of psychological distress) and the risks (eg, safety concerns) [18]. The effects of social transition on future physical and mental health continue to evolve. Longitudinal studies suggest that symptoms of anxiety and depression in TGD children improve with social and physical transition [6,39] and that, among socially affirmed children, parent- and child-reported rates of depression are similar to rates in nontransgender age- and gender-matched controls, nontransgender sibling controls, and typical rates, while rates of anxiety are only slightly higher [22,23]. In these studies, the levels of depression and anxiety symptoms were substantially lower than those reported in previous studies in children with gender diversity who were not socially transitioned [40-43].

The safety of the child or adolescent and the likelihood of acceptance in the community are important considerations in making decisions about social transition and planning. Providers can help youth and families make positive and successful social transition plans by:

- Helping them plan for disclosure to family, friends, and social contacts
- Educating staff and students within the school system
- Creating plans for safety, responses to bullying, and other social biases

- Providing medical documentation for name change, gender change, and other official documents; the TransYouth Family Allies website, among others, provides information about what to include in the medical documentation

These suggestions are discussed separately. (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Role of the medical provider'.)

Different communities approach gender diversity differently. Although some are supportive, there are others in which a fully disclosed transition of gender expression may be considered hazardous for the youth's well-being. However, it is important that parental assessment of the potential for danger is accurate. For parents who are unsure or have difficulty accepting their TGD child, safety concerns may be used to delay social transition and medical affirmation options. Families can contact a number of local or national social and advocacy agencies to assist in making a safety assessment or in facilitating social transition in school and other settings. Such organizations work with schools, teachers, and students to assist in developing plans for use of bathroom and locker room accommodations, registration questions, and overall education about gender-related issues. The involvement of these agencies allows parents to focus on parenting their TGD child rather than bringing about social change. (See 'Resources' below.)

**Hormonal interventions** — Hormonal interventions (eg, suppression of endogenous puberty and/or initiation of gender-affirming hormones to alter secondary sexual characteristics) may be beneficial for adolescents with gender diversity and strong feelings of gender dysphoria after the onset of puberty [1]. These interventions are discussed in detail below. (See 'Overview of hormonal interventions for adolescents' below.)

**Surgical interventions** — Many youth and parents have questions about surgical interventions for gender confirmation. It is important to respond to these questions, acknowledge the possibility of surgical intervention in the future, and to make referrals as necessary when youth reach a stage when surgery may be appropriate. However, for children and early adolescents, it is also important to redirect the focus to social and medical interventions. Early identification and intervention affirming TGD children may help to avoid invasive gender confirmation surgeries in the future. While most genital surgeries are performed after individuals reach the age of majority, chest dysphoria (distress about a female chest contour) is debilitating for many transmasculine youth, and chest reconstruction during adolescence is common [44]. (See 'Surgical interventions' below.)

## APPROACH IN PREPUBERTAL CHILDREN

**General suggestions** — The trajectory of gender diversity in prepubertal children is unpredictable for some children [45-47]. Others have consistent, persistent, and insistent gender-diverse identities or expression. In either case, children who live as their authentic selves and who feel safe, loved, and accepted in their homes by their caregivers have better health outcomes [22]. (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Prepubertal children'.)

Thus, it is reasonable for the primary care provider to offer education, support, and referrals as indicated [3,6,48]:

- Educate parents about the possible gender and psychosexual trajectories.
- Encourage a wide range of interests, activities, and friend groups.

  Work with leaders in youth settings to decrease the focus of arbitrarily gendered activities or attributes (eg, basketball is for boys, dance is for girls; boys are brave and girls are sensitive).
- Follow the child's lead with respect to gender expression, but set limits as necessary for safety; children who have severe gender dysphoria usually are skilled at articulating their need to present in the gender role that feels correct for them.

  Some prepubertal children who exhibit consistent, persistent, and insistent gender diversity or gender and body dysphoria pursue a social transition; prepubertal children who are experimenting with gender play or have less intense gender dysphoria are less likely to endorse transgender or other gender-diverse identities in adolescence and adulthood; much of a child's ability to express gender authentically depends upon the parents' and family's openness to a broader gender spectrum and expression [49]. (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Prepubertal children' and 'Social affirmation and transition' below.)
- As our understanding of the wide range of diversity and nonbinary identities unfolds, it is important to allow for less traditional genders to evolve in an organic and supported way. It is also important to tolerate ambivalence about gender (eg, transition, affirmation, goals) and not use it as a reason to hinder gender exploration or affirmation.
- Protect the child against negative reactions from others.
- Address concomitant emotional, behavioral, or family problems that may (or may not) have an impact on the child's feeling of acceptance in a family or on their gender

dysphoria. Encourage parents to seek mental health and other supports for themselves so that they may privately process their feelings and responses to their child.

Additional suggestions for education and support are provided separately. (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Education and support'.)

**Social affirmation and transition** — Most medical and mental health professionals agree that the approach to social affirmation in prepubertal children should be individualized for each child; that the parents' role is to support what is best for the child [48,50]; and that all children are more likely to have a healthy self-image, self-esteem, and general well-being when their authentic identity is recognized, supported, and loved. It is not uncommon for providers to meet families with socially transitioned prepubertal children who made the decision without medical input [28]. For these youth and families, medical and mental health professionals can provide additional information and resources to support and create a plan for upcoming puberty. (See 'Resources' below.)

Although evidence is insufficient to predict the long-term outcomes [16], clinical observation suggests that social transition and affirmation among children age 6 to 14 years decreases anxiety and depression [23]. In the experience of the authors of this topic review, social transition and affirmation are beneficial for many prepubertal children with persistent, strong diverse gender identity who have difficulty functioning adequately in their familial, social, and educational domains without being allowed to express their authentic gender identity. The potential for negative response and safety concerns (including bullying, harassment, rejection, isolation, and violence) must be balanced with the child's becoming incapacitated by living inauthentically. (See 'Social transition' above.)

## APPROACH IN PUBERTAL CHILDREN AND ADOLESCENTS

Gender dysphoria that persists through the onset of puberty or is increased at the onset of puberty is unlikely to subside [1,3,51]. Supportive and affirming care can be provided in a variety of settings. Many youth benefit from multidisciplinary gender specialty programs that include medical, mental health, and social work services [14,16,18]. However, access to multidisciplinary centers may be limited. As more providers become informed, trained, and adept at working with gender and sexual minorities, youth and families may have additional options for care within primary care and community mental health venues [28].

Given the spectrum and fluidity of gender identity, the management needs and goals differ from adolescent to adolescent. Adolescents may change their transition goals and requests for treatment over time according to personal desire and circumstance. Some gender-diverse youth do not desire a phenotypic transition and are content with their endogenous

hormones. They may identify as transgender, or they may identify as something different (eg, "gender fluid," "gender creative"). It is important for providers to try to understand the individual needs of each patient within the context of human development and diversity. (See 'Youth with nonbinary gender identity' below and "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Terminology'.)

**Youth with binary gender identity** — To allow time for the adolescent to develop the maturity necessary to make a thorough and informed decision about permanent physical changes, some youth may progress from nonmedical reversible adaptations that express their internal gender identity, such as changes in hair, clothing, name, and pronoun. Others may want more information and opt for partially reversible interventions (eg, gender-affirming hormones) to irreversible interventions (eg, surgical).

However, not all affirmative care starts with social transition. Some youth are uncomfortable making changes in their gender presentation before undergoing hormonal intervention because of fear of harassment, bullying, and physical violence. It is important for providers to honor the needs of each youth and to understand the strategic decision-making that allows the youth to feel most comfortable and safe. Youth who make the decision to socially transition after starting hormones should not have their care delayed. (See 'Guiding principles' above and 'Social transition' above and 'Overview of hormonal interventions for adolescents' below.)

**Youth with nonbinary gender identity** — There are increasing numbers of youth presenting for gender services who have gender identities that are neither male nor female, and do not conform to expected social standards but are somewhere in between or other. These youth may identify as "agender," "bigender," "gender fluid," "gender queer," "gender blender," or something else entirely. Although there has been no published information about using hormones to induce partial development of secondary sexual characteristics, clinicians who see large numbers of TGD youth report an increase in patients who are interested only in male chest reconstruction or testosterone suppression. There is increasing interest in adapting gender care for gender-diverse youth who may not continue with estradiol or testosterone [52].

The challenge of the care team is to work with youth to determine how they want to present their experienced gender to the outside world. Nonbinary-identified youth require providers who are open-minded and skilled at eliciting information that differentiates gender identity from gender expression and can work with youth to develop interventions that meet their individual needs [25,53]. Depending upon their level of discomfort related to the mismatch between gender identity and anatomic sex, youth with a nonbinary gender identity may or may not want to take gender-affirming hormones; some may desire a low-level dose to maintain a more androgynous effect.

## OVERVIEW OF HORMONAL INTERVENTIONS FOR ADOLESCENTS

**Potential indications** — Hormonal interventions to suppress puberty and/or promote development of cross-gender secondary sexual characteristics may be beneficial in TGD youth whose assertion of gender identity being different from their designated sex at birth is persistent, consistent, and intensifies with the onset of pubertal changes [1,6,14,49,51,54]. Pubertal suppression also may be beneficial for youth who are exploring a nonbinary identity and have concerns about the irreversible changes of endogenous puberty. Youth with intense feelings of gender dysphoria are at risk for adverse psychosocial outcomes. (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Associated concerns'.)

Additional considerations for starting hormonal therapy may include adequate psychosocial support, understanding of the expected outcomes and medical and social benefits and risks of treatment, and whether mental health counseling would be beneficial to the patient. For individuals with adverse mental health sequelae of gender dysphoria that impairs self-esteem and function (eg, activities of daily living), hormonal treatment requires close collaboration with mental health providers. These recommendations are outlined in the Endocrine Society Clinical Practice Guideline and the World Professional Association for Transgender Health (WPATH) Standards of Care, and are similar to recommendations for cisgender youth who are experiencing distress [14,16].

**Counseling and consent** — As with the initiation of any medical therapy, youth considering hormonal therapy for gender dysphoria and their parents must be fully informed of the potential benefits and risks of such therapy before they can provide informed consent. Mental health benefits and risks are a crucial part of this discussion. (See 'Monitoring during pubertal suppression' below.)

Medical contraindications to hormonal therapy are rare in periadolescents, adolescents, and young adults.

**Reversibility** — The effects of gender-affirming hormones are considered partially reversible, in contrast to social transition and gonadotropin-releasing hormone (GnRH) analogs, which are completely reversible. The irreversible effects of gender-affirming hormones often are highly desired (eg, lower voice, male pattern hair, and clitoromegaly for transmasculine youth; breast development for transfeminine youth). These more permanent effects occur gradually, giving clinicians and patients the ability to periodically review how the changes impact the patient's gender identity and feelings of dysphoria. (See 'Suppression of endogenous puberty' below and 'Gender-affirming hormone therapy' below.)

**Fertility considerations** — When counseling parents and TGD youth, it is important to emphasize:

- When TGD persons engage in sexual activity that involves egg and sperm, pregnancy can occur.

  Contraception is recommended for TGD persons who wish to avoid pregnancy [55,56]. For transmasculine individuals, long-acting reversible contraception (eg, intrauterine device, etonogestrel implant) has superior efficacy and may have desirable side effects such as amenorrhea. (See "Contraception: Issues specific to adolescents", section on 'Long-acting reversible methods'.)

- Gender-affirming hormones may compromise the ability to have a genetic child in those whose endogenous puberty was suppressed early in puberty.

  TGD youth who are treated with GnRH analogs to suppress endogenous puberty in Tanner stage 2 and then switched to gender-affirming hormones will not develop sperm or oocytes that are viable for reproduction [57]. It is not clear how gender-affirming hormones affect fertility in TGD youth who do not undergo pubertal suppression and initiate gender-affirming hormones later in puberty. However, TGD adults have successfully had genetic children [56,58].

  Transgender persons who wish to optimize their potential for genetic children should consult with a reproductive endocrinologist or urologist regarding their options for fertility preservation (eg, oocyte or sperm preservation, cryopreservation of ovarian or testicular tissue) [57,59-62]. Fertility preservation is expensive and not usually covered by insurers, which limits availability. (See "Fertility and reproductive hormone preservation: Overview of care prior to gonadotoxic therapy or surgery" and "Fertility preservation: Cryopreservation options".)

Adolescents generally are able to weigh the pros and cons of hormone therapy, including the potential impact on future fertility. In the authors' experience, many transgender youth state that their desire to express their gender authentically supersedes their desire for fertility. They clearly articulate plans to parent, but in their identified gender and using resources such as adoption or reproductive technologies. A survey of 156 TGD adolescents supports the authors' experience: 70 percent expressed interest in adoption and 36 percent in biologic parenthood [63].

**Availability of care** — Hormonal interventions for youth with gender dysphoria may be provided in a variety of settings. Specialized centers with multidisciplinary teams offer coordinated services and may be involved in long-term follow-up and research that will add to the growing body of evidence regarding outcomes [20]. However, it can be difficult for

TGD adolescents and their families to find or access care with appropriately trained medical and mental health providers [6,18,64]. Multidisciplinary centers are available in a limited number of cities. Insurance coverage for medical interventions varies geographically, and ability to pay out-of-pocket for services that are not covered by insurance may influence treatment options [65,66]. Adolescents who are unable to afford or access hormonal interventions may decide to purchase hormones online or on the street and use them without medical supervision [67,68].

When gender specialty centers are not available (which is more often than not), the WPATH standards of care recommend that the clinician providing and monitoring hormonal treatment be well versed in the relevant medical and psychological aspects of treatment [16]. Such clinicians may be board-certified endocrinologists or adolescent medicine specialists, but many gender specialists have other medical backgrounds with additional training in gender and sexual health and adolescent health. Without additional training and expertise, most primary care providers are uncomfortable with initial evaluations and starting youth on hormones. However, in order to improve access and patient-centered care, primary care providers are instrumental in coordinating care, providing referrals, and providing clinical and laboratory monitoring for patients receiving hormonal interventions. In addition, given the prior relationship with a child and family, primary care providers can be powerful role models for support, positive regard, and acceptance of transition for the youth and family members [69]. (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Role of the medical provider'.)

### Suppression of endogenous puberty

**Rationale** — Suppression of endogenous puberty may be warranted for TGD youth with persistent gender dysphoria that intensifies after the onset of puberty and nonbinary gender-diverse youth who are in the process of determining their gender identity [1,6,14,51,54].

Gender dysphoria that has been present since childhood and intensifies with the onset of puberty rarely subsides [1,3,51]. In prospective follow-up of a cohort of 70 gender dysphoric youth who underwent pubertal suppression, all of the patients elected to proceed with gender-affirming hormones [4].

Suppression of puberty may spare TGD youth from increased body dysphoria due to development of the "wrong" and often permanent sex characteristics [70], which may be associated with comorbid symptoms or risky behaviors (eg, depression, anxiety, self-harm, suicidality, substance use, high-risk sexual behaviors) [18,54]. Suppression of puberty also "buys time" during which the youth can more fully explore their gender identity with a trained mental health professional. They can work with the mental health professional to make a thoroughly informed decision about medications, surgeries, or other ways to

authenticate their genders and to develop resiliency tools to help them cope with the challenges of openly changing their social identity and expression in addition to the other challenges of adolescent development [71].

The reversibility of pubertal suppression may be comforting for parents who need additional time to learn more about gender diversity and care and to come to terms with a different future for their child than the one they may have envisioned [72].

The potential benefits of pubertal suppression include [1,6,14,71,73-75]:

- Prevention of the development of unwanted secondary sexual characteristics (eg, breast development, menarche/menses; voice deepening, phallic growth, spontaneous erections, unwanted male pattern hair growth), which may interfere with well-being and psychosocial functioning
- Clarification of gender identity and the degree of gender dysphoria
- Resumption of endogenous puberty if discontinued; if the decision is made to discontinue GnRH analogs, the youth will progress through endogenous puberty after approximately six months – including the development of mature sperm and follicles
- Opportunity to live in the phenotype of the affirmed gender (with concurrent social transition)
- Easier, less costly physical affirmation process with improved physical outcomes for patients who decide to proceed with gender-affirming hormone therapy and/or surgery than if they progress through endogenous puberty

Evidence from observational studies suggests that suppression of endogenous puberty may help to alleviate psychosocial distress in gender dysphoric youth [76]. In prospective follow-up of a cohort of 70 gender dysphoric youth, behavioral and emotional problems, depressive symptoms, and general functioning improved after treatment with GnRH analogs to suppress puberty [4]. However, pubertal suppression alone did not alleviate gender dysphoria, and all of the treated patients elected to proceed with gender-affirming hormones. In another observational study, all patients who underwent pubertal suppression with GnRH analogs were satisfied with their lack of pubertal development, all of those who were eligible for gender-affirming hormone treatment chose to proceed, no adverse effects were noted, and no patients took street hormones [71].

Longer-term follow-up is necessary to examine whether gender dysphoric adolescents who underwent pubertal suppression with GnRH analogs followed by gender-affirming hormones will be able to maintain their relatively good functioning in their adult years after gender-affirming surgery. In one study with long-term follow-up of 55 patients who

underwent puberty suppression (mean age 13.6 years) followed by gender-affirming hormone therapy (introduced at a mean age of 16.7 years) and gender-affirming surgery (mean age 19.2 years), gender dysphoria was alleviated in young adulthood (mean age 20.7 years) and well-being was similar to that in young adults from the general population [77]. In a cross-sectional survey, wanting and receiving puberty suppression during adolescence was associated with decreased rates of self-reported suicidality among >20,000 TGD adults (age 18 to 36 years) [78].

**Timing** — The patient's desire to halt endogenous puberty and readiness to begin treatment are primary factors when deciding when to begin pubertal suppression. Parental consent and support and whether or not the patient has entered puberty are additional factors. (See 'Counseling and consent' above.)

- **Presentation before the onset of puberty** – Administration of GnRH analogs **before** Tanner stage 2 provides no benefit and unnecessary expense. However, administration as soon as possible after puberty begins may provide relief for gender dysphoric youth who have increasing anxiety as puberty approaches. These youth should be assured that they will be closely followed so GnRH analogs can be administered as soon as they are indicated.

  Providers can confirm the onset of central puberty through physical examination and laboratory studies. Onset of central puberty is indicated by Tanner stage 2 breast buds ( picture 1A) or testicular/penile enlargement ( picture 1C). Laboratory evidence of pubertal onset is provided by levels of ultrasensitive luteinizing hormone (LH), follicular stimulating hormone, estradiol, or testosterone above prepubertal levels.

  Although early suppression of puberty may result in inadequate scrotal and penile tissue for traditional penile inversion vulvovaginoplasty techniques, in the authors' experience, the potential benefits of early suppression generally outweigh this concern for transfeminine youth. This concern is included in the discussion of benefits and risks before initiation of pubertal suppression and, later, initiation of estradiol.

- **Presentation after onset of puberty** – Although it is ideal to begin GnRH analogs at early Tanner 2, most youth do not present for medical care at or before this stage of puberty [1]. If initiated at Tanner stage 3 or 4 ( picture 1A-C), GnRH analogs may prevent continued progression of puberty, maintain androgynous physical features, cause some regression of secondary sexual characteristics, stop menses or erections, and provide psychological relief for a patient who is distressed by cisgendered development [4,14,71]. However, GnRH analogs alone provide little benefit for patients who present in late puberty, when irreversible secondary sexual characteristics are already well developed (eg, breasts, Adam's apple, voice deepening). For such patients,

gender-affirming hormone therapy may be more appropriate. (See 'Gender-affirming hormone therapy' below.)

The use of GnRH analogs in conjunction with gender-affirming hormones allows for the induction of a more peer-concordant male puberty in transmasculine individuals. For example, a 13- or 14-year-old who identifies as transmasculine and has already achieved Tanner 5 development might be a good candidate for starting testosterone, but the testosterone dose necessary to suppress menses would result in age-inappropriate masculinization. Concurrent administration of GnRH analogs would suppress menses while allowing peer-concordant masculinization through progressive testosterone dose escalation. Medroxyprogesterone acetate injections, the 52 mg levonorgestrel-releasing intrauterine device (LNg IUD), or oral norethindrone may be an alternative for menstrual suppression [79]. Both medroxyprogesterone acetate and the LNg IUD provide the added benefit of contraception, which norethindrone does not. (See "Intrauterine contraception: Candidates and device selection", section on 'Reasons to choose an LNG IUD'.)

Transfeminine individuals can also benefit from concurrent GnRH analogs and gender-affirming hormones. Reduction in androgen production by central LH suppression (via GnRH analogs) is far superior to peripheral blockade of androgen synthesis and action (eg, finasteride spironolactone). Transfeminine individuals frequently can be feminized with lower doses of estrogen if they receive concurrent GnRH analogs (regardless of sexual maturity rating).

**Regimen** — Suppression of puberty can be achieved with the use of GnRH analogs, antiandrogens, antiestrogens, and medroxyprogesterone acetate [14,76,80,81]. GnRH analogs are usually preferred because of their efficacy, safety profile, and clinical experience in treating children with precocious puberty [81-84]. (See "Treatment of precocious puberty", section on 'Formulations and dosing'.)

The availability of GnRH analogs and coverage by insurance varies geographically [65]. Medication regimens are not standardized. The protocol suggested in the Endocrine Society Clinical Practice Guideline was developed by the Center of Expertise on Gender Dysphoria (formerly the Amsterdam Gender Clinic) and is endorsed by the Australasian Paediatric Endocrine Group [14,38,71,85]. This protocol and others adapted from it have demonstrated suppression of puberty without adverse effects in small cohorts of patients [3-5].

GnRH analogs may be administered in a variety of forms, including injections and implants (table 3). In our experience, most adolescents start with the histrelin insert (effective for two years) or with intramuscular leuprolide injections every three months. The dose of the injection may be titrated to adequately suppress puberty by patient report, physical

examination, and/or laboratory values. (See 'Monitoring during pubertal suppression' below.)

GnRH analogs ideally are continued concurrently with gender-affirming hormones until patients can receive gonadectomies [14]. However, they usually are discontinued earlier. Prolonged suppressive therapy with GnRH analogs is expensive, may not be covered by insurance, and may be unaffordable or unavailable for patients [65,75]. Alternatives to the ideal regimen include either:

- Continuing GnRH analogs over one to two years as gender-affirming hormone doses are titrated and approach adult levels, or
- Discontinuing GnRH analogs after one to two years and while quick-starting adult-dose gender-affirming hormone therapy

Timing of gender-affirming hormone administration and puberty in the youth's identified gender generally should be aligned with puberty initiation and development consistent with their peers, although the youth's height goal is another consideration. (See 'Timing' below.)

**Monitoring during pubertal suppression** — Monitoring youth during pubertal suppression allows providers to assess mental and physical health, to counsel about potential adverse effects, and to continue to discuss the affirmation plan with youth and their families. Parameters to be monitored include:

- **Growth (height, weight**) – Pubertal suppression alters the timing of the pubertal growth spurt and delays fusion of the growth plates, which may affect adult height [71,76].

  Monitoring height (including height velocity and height curves) every three months during pubertal suppression can help to achieve the youth's height goals (eg, prevention of excessively tall stature for transfeminine patients, optimized height for transmasculine patients). Weight should also be monitored regularly because unwanted weight gain may occur with the use of GnRH agonists.

  We do not monitor bone age (eg, radiograph of the left hand). However, some experts obtain bone age annually in youth who are concerned about final height. Bone age radiographs and timing of closure of epiphyseal plates can help determine where the youth is in their growth trajectory.

- **Pubertal progression** – Asking whether puberty is progressing is the most important way to monitor the effectiveness of pubertal suppression therapy.

  Providers may measure endogenous sex hormone levels (using ultrasensitive estradiol or testosterone assays) and gonadotropin levels (using pediatric LH assays) at baseline

and every six months to assure adequate suppression into the prepubertal range (which may vary from laboratory to laboratory) or to reassure patients that suppression is effective. Ultrasensitive sex steroid levels are the best indicator of suppression.

Measurement of endogenous sex hormone levels and gonadotropin levels is also warranted if patients report symptoms of pubertal change. If the gonadal axis is not completely suppressed, the interval between GnRH analog injections may need to be shortened or the dose increased.

- **Bone health** – Decreased bone mineral density (BMD) is a potential risk of pubertal suppression because accretion of BMD is suspended during GnRH analog therapy without gender-affirming hormones. There is limited information about long-term bone health among TGD youth who are treated with GnRH analogs and gender-affirming hormones or whether maintaining physiologic levels of gender hormones in adulthood is associated with improved BMD. In observational studies of TGD youth treated with GnRH analogs, BMD increased after addition of gender-affirming hormones, partially compensating for decreased accretion during GnRH analog therapy [71,86,87]. Similarly, in children treated with GnRH analogs for precocious puberty, bone mass is regained after cessation of treatment and peak bone mass is normal. (See "Treatment of precocious puberty", section on 'Monitoring'.)

  The authors of this topic review do not monitor BMD for most TGD youth who are treated with GnRH analogs. However, TGD youth with restrictive eating disorders, chronic glucocorticoid use, or other risk factors for decreased BMD or osteoporosis may benefit from monitoring BMD over time, particularly if they may receive GnRH analogs without gender-affirming hormones for ≥2 years. Addition of gender-affirming hormones may be warranted if bone density z score decreases substantially, although other factors are more important in the decision to initiate gender-affirming hormones. (See 'Timing' below.)

  We do not monitor vitamin D levels but recommend vitamin D and calcium supplementation for adolescents (independent of gender identity) with risk factors for vitamin D deficiency (eg, insufficient intake, poor sunlight exposure, dark skin). Other experts may measure vitamin D levels and prescribe vitamin D to patients with documented low levels to encourage adherence with supplementation. (See "Vitamin D insufficiency and deficiency in children and adolescents".)

- **Mental health and other effects related to hormonal changes** – Patients undergoing pubertal suppression should be monitored regularly for mental health and other effects related to hormonal changes:

- Transmasculine and transfeminine patients who are started on GnRH analogs well into puberty (ie, Tanner stage 3 to 5) may experience hot flashes, mood disruption, and loss of libido [76].

- Transmasculine patients also may have signs and symptoms related to rapid withdrawal of sex hormones (eg, withdrawal bleeding and disruption of menstrual cycles) [71]. Patients and parents should be alerted to potential irritability, depression, and other symptoms of menopause [88].

Patients with serious mental health effects must be monitored closely (eg, depression). In the authors' experience, it is beneficial to prepare patients for potential changes in feelings or thoughts related to hormonal interventions – starting with the probable positive changes (eg, relief, decreased hopelessness, decreased suicidality) followed by the less likely negative changes (eg, irritability, moodiness, fatigue). This discussion also makes explicit the need for accurate reporting of adverse mental health effects.

### Gender-affirming hormone therapy

**Rationale and indications** — Treatment with gender-affirming hormones is necessary to induce cross-gender pubertal development and to maintain cross-gender phenotypic appearance. Some of the phenotypic changes that are attained with gender-affirming hormone therapy are reversible and others are not. (See 'Transfeminine persons' below and 'Transmasculine persons' below.)

Additional considerations before initiation of gender-affirming hormonal therapy include ensuring that the adolescent [14,16]:

- Has adequate psychosocial support.

- Assents to treatment, understanding the expected outcomes and the medical and social risks and benefits (as with any medication); some centers require a letter from a mental health provider who has determined that the youth would benefit from gender-affirming hormonal therapy; others centers do not.

- Will take gender-affirming hormones in a responsible manner (as with any medication).

- Has no contraindications to gender-affirming hormones (most of which are uncommon in adolescents):

  - For transfeminine patients, estrogen-sensitive tumors are a contraindication; increased risk for venous thromboembolism (VTE) and severe liver dysfunction are precautions.

Coexisting medical problems that increase baseline risk of VTE are usually not considered contraindications to estradiol because there are no other medication options for feminizing therapy. The potential (but unquantifiable) risk of VTE must be balanced with the **known** risks of negative health outcomes (eg, self-harm, suicide) in transgender individuals who are not supported in their transition. (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Associated concerns'.)

Treatment plans should focus on efforts to minimize other VTE risk factors. Women with migraine with aura or other neurologic symptoms, uncontrolled hypertension, and other conditions that cause excessive blood clotting should understand that the relative risk of VTE is increased with use of estradiol but that the absolute risk of VTE for each individual patient is unknown. Gender-affirming hormone therapy with 17-beta estradiol is administered at physiologic doses and considered less thrombogenic than the supraphysiologic doses of ethinyl estradiol in the original studies identifying increased risk of VTE for hormone replacement therapy or contraception [89,90]. When prescribing 17-beta estradiol for gender-affirming therapy, providers can minimize the risk of VTE by using nonoral routes (eg, dermal, sublingual, injectable).

- For transmasculine patients, testosterone-sensitive tumors, pre-existing problematic polycythemia, and severe chronic liver dysfunction are contraindications.

These requirements are outlined in the Endocrine Society Clinical Practice Guideline [14] and the WPATH Standards of Care [16].

**Timing** — The decision about when to initiate gender-affirming hormones in adolescents must be individualized.

- **Adolescents who have undergone pubertal suppression** – For adolescents who have undergone pubertal suppression, protocols from the Netherlands recommend initiation of gender-affirming hormones to induce cross-gender puberty at age 16 years, which is the legal age of consent in the Netherlands and several other European countries [1,3,14,18,71]. The guidelines from the Endocrine Society acknowledge that "there are compelling reasons to initiate gender-affirming hormones before age 16 years" [14]. Earlier initiation may be warranted for certain patients, including:
  - Those whose gender identity is well established and stable at an early age
  - Pubertal adolescents who report gender dysphoria, a transgender identity, or a gender identity that would benefit from gender-affirming hormones

- Transfeminine patients with tall stature (for earlier closure of the growth plates)

Initiation of gender-affirming hormones at a time similar to pubertal onset in age-matched peers (ie, before 16 years of age) may have psychosocial benefits. Given the importance of peer congruence during the high school years, it is reasonable to assume that a 16 year old with the sexual development of a 10 year old may suffer some psychological distress – although this has not been formally evaluated in clinical studies. Observational studies suggest that constitutional delay of growth and puberty is associated with adverse psychosocial effects, including [91]:

- Incompetence and vulnerability
- Impaired self-esteem
- Reluctance to participate in athletic activities
- Social isolation
- Impaired academic performance
- Substance abuse
- Disruptive and suicide behavior

Initiation of gender-affirming hormones that is more congruent with peers' average age of puberty (ie, age 12 to 13 years for females and age 13 to 14 years for males) also can decrease the financial burden for patients and families if suppression of puberty with GnRH is discontinued when gender-affirming hormones are started. In the United States (where triptorelin is not a labeled indication for pubertal suppression), suppression of puberty with GnRH analogs is more expensive than gender-affirming hormones and may not be covered by insurance [65], whereas gender-affirming hormones often are covered by insurance plans or available at the substantially discounted medication programs offered by various national pharmacies.

- **Adolescents who have not undergone pubertal suppression** – Adolescents with gender dysphoria who have not undergone pubertal suppression may begin gender-affirming hormone therapy if they would benefit from gender-affirming hormones, have a healthy and safe affirmation plan, and are ready to begin their second puberty [1,18]. (See 'Rationale and indications' above.)

  If gender-affirming hormone therapy is started after puberty is complete or near-complete in transfeminine youth, the administration of estrogen and androgen blockers will not affect voice pitch, laryngeal prominence (Adam's apple), height, and skeletal features, or eliminate male pattern facial and body hair [18]. Similarly, if gender-affirming hormone therapy is started after puberty is complete or near-complete in transmasculine youth, the administration of testosterone will not reduce the size of or remove breast tissue.

The development of undesired, permanent phenotypic characteristics highlights the importance of screening for and early identification of gender diversity in prepubertal children. Improved identification and early initiation of gender-affirming care may decrease the need for subsequent surgeries and interventions and improve the youth's ability to present physically as their asserted gender. (See "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Identification'.)

**Transfeminine persons** — Exogenous 17-beta estradiol is necessary for feminization of birth-designated males. The addition of androgen blockers (eg, spironolactone, bicalutamide, or finasteride) assists in reducing testosterone activity and/or male-pattern hair.

The primary aims of estrogen therapy are ( table 4) [14,18]:

- Development of breasts (irreversible) and female fat distribution pattern (reversible)
- Softening of the skin (reversible)
- Maintenance of a higher-pitch voice (provided that puberty was blocked; estrogen will not cause a voice change if the voice has already deepened)
- Decrease/avoidance of male pattern body and facial hair (partially reversible)
- Avoidance of masculine skeletal changes that occur with testosterone during puberty
- Decrease in testicular mass (which may make it easier to tuck the testicles into the inguinal canal; unknown if reversible)

Gender-affirming hormone regimens to induce puberty and to maintain cross-gender sexual characteristics are available from professional groups and centers of excellence for transgender care [13,14,16]. These regimens assume continued treatment with GnRH analogs. Increasing the estradiol dose gradually may prevent striae and abnormal breast shape. For patients who are not continuing GnRH analogs, the dose of estrogen will need to be increased (approximately doubled) to achieve development of female secondary sexual characteristics and suppress endogenous testosterone.

Estrogen is available in oral, sublingual, topical (patch), intramuscular and subcutaneous injections, or intradermal pellet preparations [92]. The oral formulation of 17-beta estradiol administered sublingually is most commonly used because blood levels can be monitored and it is associated with a lower risk of thromboembolic events than other estrogens (eg, ethinyl estradiol) [93]. However, some adolescents prefer injections of 17-beta estradiol every one to two weeks.

Estradiol therapy is effective in inducing breast development and female fat distribution in TGD adolescents [76]. In a review of 28 adolescents who received gender-affirming pubertal induction with estradiol for at least one year, breast development started within three months in 15 of 18 girls for whom data were available, and 12 of 14 achieved stage 4 to 5 sexual maturity rating breast development within three years [94].

There is little information about the frequency of adverse effects in adolescents receiving gender-affirming hormones [1,3,6]. In several small case series, gender-affirming estradiol therapy in adolescent patients has not been associated with severe complications or metabolic abnormalities (eg, hypertension; increased body mass index [BMI]; electrolyte disturbances; elevated creatinine, liver enzymes, lipids, hemoglobin/hematocrit, hemoglobin A1C) [74,76,94-96].

**Transmasculine persons** — Exogenous testosterone is necessary for masculinization of birth-designated females. The primary aims of testosterone therapy are ( table 5) [14,18]:

- Suppression of menstruation and breast development (reversible)
- Clitoral enlargement (irreversible)
- Deepening of the voice (irreversible)
- Development of male pattern body and facial hair (partially reversible)
- Increase in lean muscle mass (reversible)

Gender-affirming hormone regimens to induce puberty and to maintain cross-gender sexual characteristics are available from professional groups and centers of excellence for transgender care [13,14,16]. These regimens assume continued treatment with GnRH analogs. For patients who are not using or continuing GnRH analogs, the dose of testosterone will need to be increased to achieve development of male secondary sexual characteristics and suppress endogenous estrogen.

Testosterone is available as an injection (subcutaneous or intramuscular) or topically (eg, patch, gel, cream) in the United States (and orally in some countries). It is most commonly given subcutaneously on a weekly schedule. Subcutaneous administration is used by many providers because it is better tolerated, less painful, and as efficacious as intramuscular injection [97]. Intramuscular injections may be dosed every one or two weeks. Topical (and oral) preparations have unpredictable absorption, which makes dosing and monitoring difficult. Another disadvantage of topical preparations is that they may be inadvertently absorbed by another person through skin-to-skin contact, potentially causing unintended masculinization. Compounding pharmacies can create small-volume, highly concentrated creams that require daily dosing but are less likely to transfer to another person.

Another preparation of testosterone may be preferable for patients with poor adherence, needle phobia, or needle fatigue. This includes autoinjectable testosterone administered

weekly, deep intramuscular injectable testosterone administered every two to three months, or subdermally implanted testosterone pellets.

Transmasculine youth who are starting gender-affirming hormones in early or middle adolescence may not necessarily desire profuse body hair, so they may benefit from starting at a low dose and increasing slowly. On the other hand, too slow or too low a dose may not be sufficient to suppress endogenous estrogen and may allow continued and undesired menstruation or breast development.

There is little information about the frequency of adverse effects in adolescents receiving gender-affirming hormones [1,3,6]. In one case series of 39 transmasculine adolescents receiving gender-affirming hormone therapy, 12 (32 percent) developed minor adverse effects, including acne requiring treatment with isotretinoin (seven patients), male pattern baldness (one patient), mild dyslipidemia (three patients), and mood swings (one patient) [74]. However, none permanently discontinued gender-affirming hormone therapy. In another series of 72 transmasculine adolescents, testosterone therapy was associated with increased BMI and hemoglobin/hematocrit and decreased high-density lipoprotein levels, known effects that were mild and not clinically significant enough to alter therapy [95]. Gender-affirming testosterone therapy was not associated with changes in blood pressure, prolactin, electrolytes, liver function tests, or hemoglobin A1C [76,98].

Transmasculine individuals who are having receptive vaginal sex with people with penises (ie, sperm and egg sex) should be advised that testosterone administration will not prevent pregnancy even if the patient is amenorrheic. Effective contraceptives and condom use are recommended to prevent pregnancy and sexually transmitted infections (STIs). The 52 mg LNg IUD and etonogestrel implants are alternative methods of contraception that also may suppress menses but will not prevent STIs [79]. (See "Intrauterine contraception: Candidates and device selection", section on 'Which LNG IUD?' and "Etonogestrel contraceptive implant".)

Other options for contraception and factors in the choice of contraceptive method are discussed separately. (See "Contraception: Issues specific to adolescents", section on 'Choosing a method'.)

**Monitoring** — Patients undergoing gender-affirming hormone therapy should return approximately every three months for the first year of treatment to assure that their hormones are meeting desired goals, levels are within desirable physiologic ranges, and that they are avoiding untoward effects. If the patient is progressing well into their transgender puberty and having no untoward side effects, providers may decrease the frequency to every six months or year thereafter.

During the induction of puberty, the following examinations and laboratory tests are recommended:

- Height and weight – Every three months during the first year of treatment.
- Testosterone or estradiol levels – May be monitored to evaluate adequacy of dosing and/or adherence. Use of liquid chromatography/tandem mass spectrometry (if available) may reduce cross-reactivity and increase accuracy.
  - For weekly subcutaneous or bimonthly intramuscular testosterone injections, total testosterone levels should be interpreted based on the timing of the dose (eg, peak, mid, trough).
  - For patients taking estradiol-containing preparations, estradiol levels can be variable and difficult to interpret. However, measurement of estradiol levels may be helpful for patients who are taking higher-than-recommended doses of estradiol and are at risk for VTE, or for those with subtherapeutic levels who may benefit from increased doses.

  We use testosterone and estradiol levels to adjust dosing according to patient goals, clinical changes, average physiologic levels, and avoidance of side or adverse effects.
- Renal function, liver function, lipids, glucose, insulin, hemoglobin A1C – Yearly or as indicated; more frequent monitoring of these tests in TGD adolescents is not necessary solely because they are taking gender-affirming hormones but may be warranted if clinically indicated. (See 'Transfeminine persons' above and 'Transmasculine persons' above.)

  Following induction of gender-affirming puberty, we monitor patients clinically and obtain laboratory studies as clinically indicated. Observational studies suggest that liver function tests and blood chemistry are largely unaffected by gender-affirming hormone therapy in adolescents [95,98].

## SURGICAL INTERVENTIONS

Gender-affirming surgeries (formerly surgical sex reassignment) include:

- Male chest reconstruction (ie, removal of female breasts and construction of a more masculine-appearing chest) for transmasculine persons or nonbinary persons with severe chest dysphoria [44]
- Breast augmentation for transfeminine persons

- Genital reconstruction surgery:
  - Creation of a neophallus and testicular implants
  - Vulvovaginoplasty and orchiectomy

In the United States, insurance preauthorization for gender-affirming surgery in adolescents <18 years of age typically requires substantial documentation, but does occur, especially for transmasculine persons with chest dysphoria.

Gender-affirming surgery is discussed separately. (See "Transgender women: Evaluation and management", section on 'Gender confirmation surgery' and "Transgender men: Evaluation and management", section on 'Gender confirmation surgery'.)

## RESOURCES

Resources for patients, families, and providers include:

- Children's National Health System Gender Development Program
- Gender Spectrum
- National Center for Education in Maternal and Child Health at Georgetown University
- Trans Youth Equality Foundation
- TransActive
- TransYouth Family Allies
- University of California, San Francisco Center of Excellence for Transgender Health
- World Professional Association for Transgender Health

Books for children and adolescents [99]:

- It's Perfectly Normal: Changing Bodies, Growing Up, Sex and Sexual Health by Robie H. Harris and Michael Emberley (Candlewick 2009)
- Changing Bodies, Changing Lives: Expanded Third Edition: A Book for Teens on Sex and Relationships by Ruth Bell (Three Rivers Press 1998)
- Sex is a Funny Word: A Book about Bodies, Feelings, and YOU by Cory Silverberg and Fiona Smyth (Triangle Square 2015)

- Who are you? The Kid's Guide to Gender Identity by Brook Pessin-Whedbee and Naomi Bardoff (Jessica Kingsley Publishers 2016)

## SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Transgender health" and "Society guideline links: Adolescent sexual health and pregnancy".)

## SUMMARY AND RECOMMENDATIONS

- The information provided in this topic is intended to allow primary care providers to educate and support patients and families of patients with gender diversity and to coordinate care, provide referrals, and monitor patients receiving care from specialists. (See 'Overview' above.)

- Management for transgender or gender-diverse (TGD) youth is determined according to the individual's gender development, needs, and goals. The safety and well-being of the youth and their family members is foremost. (See 'Guiding principles' above.)

- Treatment options may be influenced by family expectations, cultural differences, opinions of health professionals, insurance coverage, and availability of services. We support an affirming mental health approach. Reparative therapies, which claim to "cure" transgender identity, are considered unhelpful and potentially harmful by most professional organizations. (See 'Mental health interventions' above.)

- Phenotypic interventions include social transition and affirmation (ie, living partially or completely in the preferred gender role by adapting hairstyle, clothing, pronouns, and possibly a new name) and hormonal interventions to suppress endogenous puberty and/or alter secondary sexual characteristics. (See 'Hormonal interventions' above.)

- Given the unpredictability of the trajectory of gender diversity in prepubertal children, it seems reasonable for the primary care provider to offer education, support, and referral to mental health providers as indicated for those with evidence of gender dysphoria; coexisting anxiety, depression, or suicidality; or serious interpersonal conflicts with peers (eg, bullying) or parents. (See 'Approach in prepubertal children' above and 'Indications for mental health referral' above and "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Role of the medical provider'.)

- Gender dysphoria that persists through the onset of puberty or is increased at the onset of puberty is unlikely to subside. For adolescents with gender dysphoria, most gender specialists suggest a supportive, affirming approach with an interdisciplinary team that includes medical and mental health specialists. The management needs and goals differ from adolescent to adolescent. (See 'Approach in pubertal children and adolescents' above.)

- To allow time for the adolescent to develop the maturity necessary to make a thorough and informed decision about permanent physical changes, medical interventions generally progress from reversible (eg, social transition, pubertal suppression), to partially reversible interventions (eg, gender-affirming hormones), to irreversible interventions (eg, surgical interventions). (See 'Approach in pubertal children and adolescents' above and 'Social transition' above and 'Overview of hormonal interventions for adolescents' above.)

- Hormonal interventions to suppress puberty and/or promote development of cross-gender secondary sexual characteristics may be beneficial for TGD youth whose desire to be of the other gender is persistent, consistent, and intensifies with the onset of pubertal changes and for youth who are exploring a nonbinary identity with concerns about potential irreversible changes if they immediately proceed on time through their endogenous puberty. (See 'Potential indications' above.)

- Early identification and support may promote safety and health for TGD youth. Intense feelings of gender dysphoria and lack of access to gender-affirming medications and parental support are associated with adverse long-term psychosocial and health outcomes. (See 'Potential indications' above and "Gender development and clinical presentation of gender diversity in children and adolescents", section on 'Associated concerns'.)



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Topic 86771 Version 48.0

## GRAPHICS

### Terms used to describe various aspects of gender and sexuality*

| | |
|---|---|
| **Gender identity** | An individual's innate sense of feeling male, female, neither, or some combination of both. |
| **Natal or birth-assigned/birth-designated sex** | Typically assigned/designated according to external genitalia or chromosomes. |
| **Gender expression** | How gender is presented to the outside world (eg, feminine, masculine, androgynous); gender expression does not necessarily correlate with birth-designated sex or gender identity. |
| **Gender diversity** | Variation from the cultural norm in gender identity, expression, or gender role behavior (eg, in choices of toys, playmates); "gender diversity" acknowledges the spectrum of gender identities and replaces "gender nonconformity," which has negative and exclusionary connotations. |
| **"Transgender" ("trans" as an abbreviation)** | Umbrella term that is used to describe individuals with gender diversity; it includes individuals whose gender identity is different from their birth-designated sex and/or whose gender expression does not fall within stereotypical definitions of masculinity and femininity; "transgender" is used as an adjective ("transgender people"), not a noun ("transgenders"). |
| **Gender dysphoria or incongruence** | Distress or discomfort that may occur when gender identity and birth-designated sex are not completely congruent. |
| **Transsexual** | Older, clinical term that has fallen out of favor; historically, it was used to refer to transgender people who sought medical or surgical interventions for gender affirmation. |
| **Sexual orientation** | An individual's pattern of physical and emotional arousal (including fantasies, activities, and behaviors) and the gender(s) of persons to whom an individual is physically or sexually attracted (gay/lesbian, straight, bisexual); sexual orientation is an entirely different construct than gender identity, but is often confused with it; the sexual orientation of transgender people is based upon their identified gender (eg, a transgender man who is attracted to other men might identify as a gay man; a transgender woman who is attracted to other women might identify as a lesbian). |
| **Sexual behaviors** | Specific behaviors involving sexual activities that are useful for screening and risk assessment; many youth |

| | |
|---|---|
| | reject traditional labeling (homosexual, heterosexual, bisexual) but still have same-sex partners. |
| **Transgender man/transman/transmasculine person** | Person with a masculine gender identity who was designated a female sex at birth. |
| **Transgender woman/transwoman/transfeminine person** | Person with a feminine gender identity who was designated a male sex at birth. |
| **Nonbinary gender identity** | Person of any birth-designated sex who has a gender identity that is neither masculine nor feminine, is some combination of the two, or is fluid. Other terms that may be used for nonbinary gender identity include genderqueer, gender creative, gender independent, bigender, noncisgender, agender, two-spirit, third sex, and gender blender. |

* These are cultural and descriptive terms, not diagnostic terms, which are specific to medical and pathology-based paradigms.

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Graphic 86993 Version 12.0

## Examples of ways that youth, providers, and caretakers can assist gender diverse youth create a transition plan according to youth, family/parent, and provider priorities

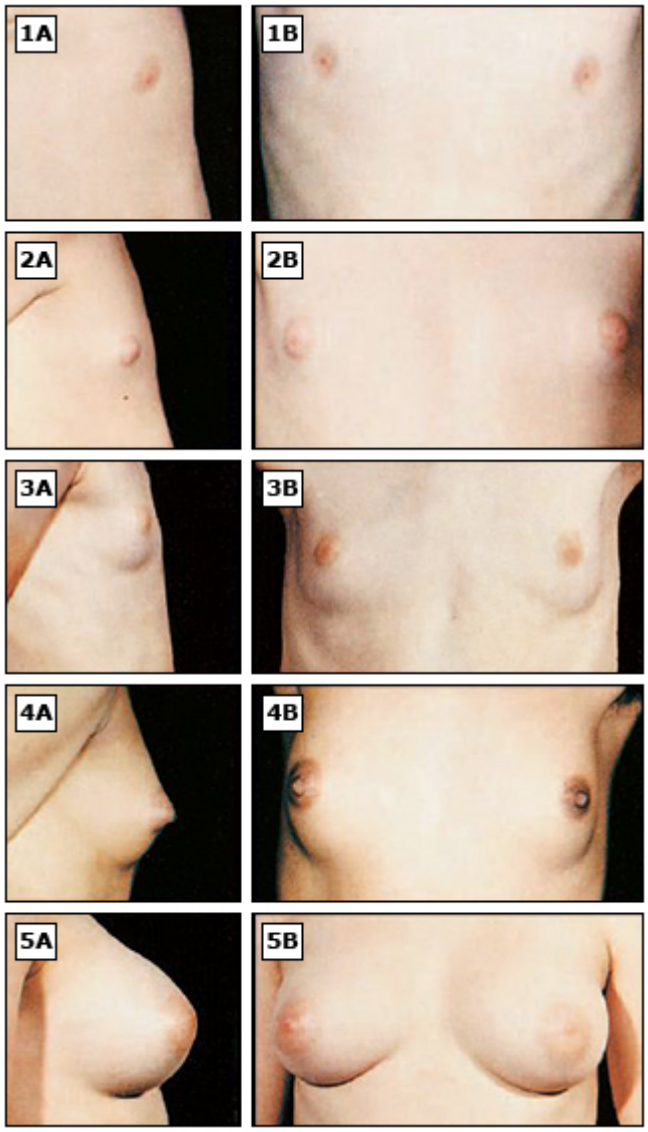
| Goal (examples) | Specific action(s) | | |
|---|---|---|---|
| | **Youth** | **Family/parent** | **Therapist/other child health professionals** |
| **Youth priorities** | | | |
| Be allowed to dress in the gender they assert | ▪ Pick out clothes that express asserted gender and are school and age appropriate | ▪ Assist the youth with in-store, online shopping<br>▪ Allow the youth to cut hair in style they want | ▪ Reassure parents that allowing a youth to express their asserted gender is generally desirable for self-esteem and identity development |
| Be called by asserted name and pronouns | ▪ Tell friends that you would like them to use your asserted name and desired pronouns | ▪ Make using asserted name a priority for self and family members; apologize and try again when mistakes are made<br>▪ Engage with school, peers and parents, and other family and social settings to introduce and find ways to maintain change in name and pronouns | ▪ Impress upon parents and others that use of the asserted name and pronouns is very important to the youth; it sends the youth a message that their identity is acknowledged and that their needs are important |
| **Family/parent priorities** | | | |
| Help the youth disclose at a time and in a manner that allows parents to prepare important support persons | ▪ May need to delay full social transition until parents have talked to and prepared other support persons | ▪ Work with teachers, guidance office, and principal to create plan for disclosure to peers | ▪ Work with schools to increase their knowledge of gender-diverse youth and needs specific to this youth and family |

| | | | |
|---|---|---|---|
| | ▪ Can fully social transition at home with support of parents<br>▪ Consider and tell parent if there are any persons who might make transition unsafe | ▪ Have plan for supporting the youth when there are negative reactions to disclosure | ▪ Engage agencies that may help parents by taking the role of advocate so that parents can maintain role of caregiver |
| Maintain plans for safety with potential for bullying and assault | ▪ Be alert to persons or situations that present as negative or threatening regarding their gender expression<br>▪ Immediately report to teacher and parent(s) if persons are bullying or threatening | ▪ Discuss with principal and school zero tolerance policies on bullying and assault<br>▪ Consider which past and present persons and settings may be negative or harmful to the youth's transition goals | ▪ Work with youth and parents regarding healthy ways to express self, react to negative social interactions, and maintain safety with persons who are not supportive or intolerant |
| **Mental health provider priorities** | | | |
| Prevent self-harm and suicide | ▪ Agree to safety plan with therapist | ▪ Know safety plan and be one of the responsible adults to whom the youth can report suicidal or self-harm thoughts | ▪ Encourage total honesty and disclosure when discussing self-harm, suicidality, and suicide attempts; review and revise safety plan as needed |
| Family/parent acceptance | ▪ Understand that parents and other families may "transition" and accept their identity in a somewhat different time frame than theirs | ▪ Be open to individual, couples, or family therapy to learn how to adapt to the youth's asserted identity and cope with their own feelings | ▪ Assist parents, siblings, and additional significant caregivers with their own thoughts and feelings with the transition plan |

*Courtesy of Michelle Forcier, MD, MPH, and Johanna Olson-Kennedy, MD.*

Graphic 87390 Version 7.0

## Sexual maturity rating (Tanner staging) of breast development in females




Stages in breast development in females.

Stage 1 – Prepubertal, with no palpable breast tissue.

Stage 2 – Development of a breast bud, with elevation of the papilla and enlargement of the areolar diameter.

Stage 3 – Enlargement of the breast, without separation of areolar contour from the breast.

Stage 4 – The areola and papilla project above the breast, forming a secondary mound.

Stage 5 – Recession of the areola to match the contour of the breast; the papilla projects beyond the contour of the areola and breast.

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*Figure from: Roede MJ, van Wieringen JC. Growth diagrams 1980: Netherlands third nation-wide survey. Tijdschr Soc Gezondheids 1985; 63:1. Reproduced with permission from the author.*

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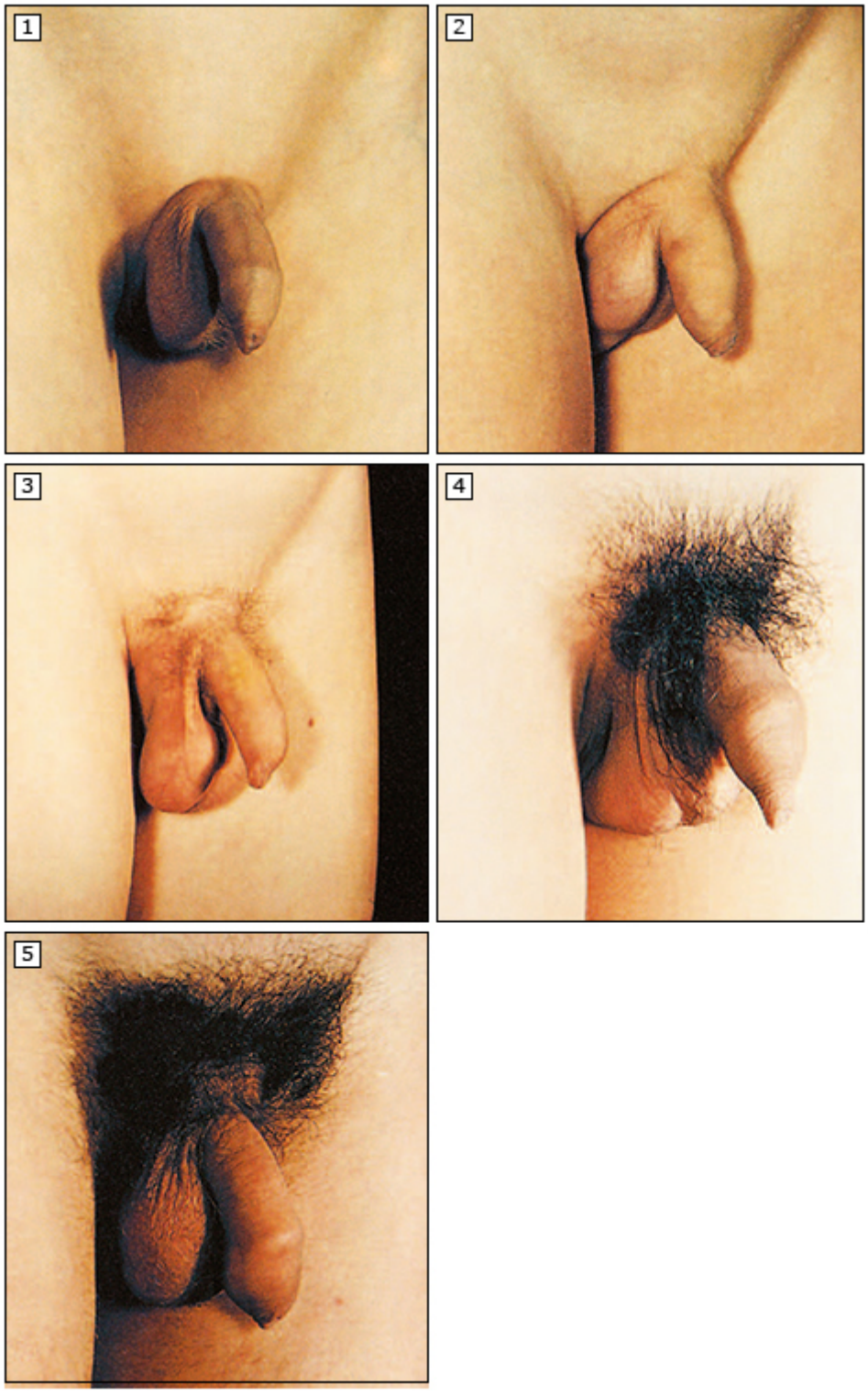
Graphic 72038 Version 10.0

## Sexual maturity rating (Tanner staging) of pubic hair and external genitalia development in males




Stages of pubic hair development in males:

- Stage 1 – Prepubertal, with no pubic hair.
- Stage 2 – Sparse, straight pubic hair along the base of the penis.
- Stage 3 – Hair is darker, coarser, and curlier, extending over the mid-pubis.
- Stage 4 – Hair is adult-like in appearance but does not extend to thighs.

- Stage 5 – Hair is adult in appearance, extending from thigh to thigh.

Stages of external genitalia development in males:

- Stage 1 – Prepubertal.
- Stage 2 – Enlargement of testes and scrotum; scrotal skin reddens and changes in texture.
- Stage 3 – Enlargement of penis (length at first); further growth of testes.
- Stage 4 – Increased size of penis with growth in breadth and development of glans; testes and scrotum larger and scrotal skin darker.
- Stage 5 – Adult genitalia.

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*Figure from: Roede MJ, van Wieringen JC. Growth diagrams 1980: Netherlands third nation-wide survey. Tijdschr Soc Gezondheids 1985; 63:1. Reproduced with permission from the author.*

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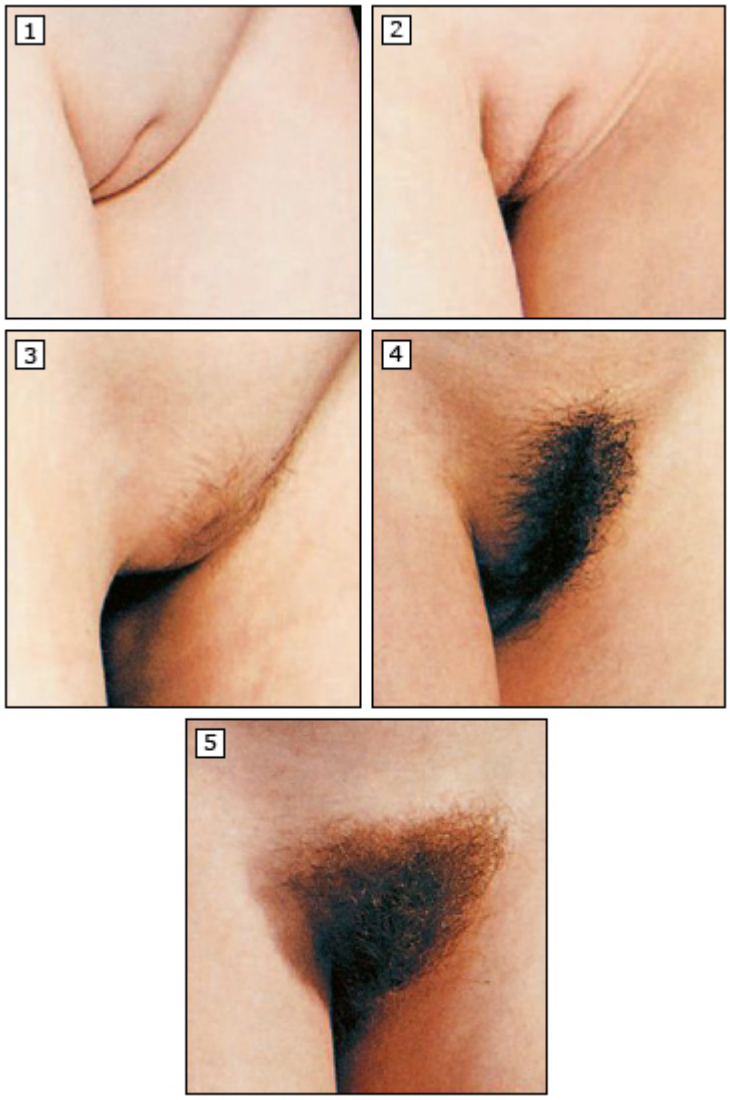
Graphic 80005 Version 8.0

## Sexual maturity rating (Tanner staging) of pubic hair development in females




Stages of development in pubic hair in females.

Stage 1 – Prepubertal with no pubic hair.

Stage 2 – Sparse, straight hair along the lateral vulva.

Stage 3 – Hair is darker, coarser, and curlier, extending over the mid-pubis.

Stage 4 – Hair is adult-like in appearance, but does not extend to the thighs.

Stage 5 – Hair is adult in appearance, extending from thigh to thigh.

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*Figure from: Roede MJ, van Wieringen JC. Growth diagrams 1980: Netherlands third nation-wide survey. Tijdschr Soc Gezondheids 1985; 63:1. Reproduced with permission from the author.*

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Graphic 79782 Version 7.0

## Long-acting gonadotropin-releasing hormone agonists for treatment of central (gonadotropin-dependent) precocious puberty

| GnRH agonist | Trade names and availability | Dose, frequency, and method of administration |
|---|---|---|
| Histrelin acetate subcutaneous implant | Supprelin LA (US) | Subcutaneous implant. Children ≥2 years – 50 mg implant surgically inserted every 12 months. Releases approximately 65 mcg per day over 12 months. |
| Leuprolide acetate (leuprorelin) | Lupron Depot-Ped (1 month) (US)<br>Lupron Depot CPP (CAN)<br>Lucrin (EU, AU, SA, elsewhere) | Intramuscular depot injection, given every 28 days.<br>Available strengths:<br>▪ 3.75, 7.5, 11.25, or 15 mg<br>Starting doses vary among countries:<br>▪ US – 7.5 to 15 mg<br>▪ Europe and Asia – 3.75 mg<br>Weight-based dosing is no longer recommended. |
| | Lupron Depot-Ped (3 month)<br>Lucrin Depot Paediatric (3 month) (AU) | Intramuscular depot injection, given every 3 months.<br>Available strengths:<br>▪ 11.25 or 30 mg<br>Criteria for selection of the 11.25 mg versus 30 mg dose have not been established. |
| | Fensolvi (6 month) (US) | Subcutaneous injection, to be administered by a health professional, given every 6 months. Approved by the US FDA for children ≥2 years with central precocious puberty.<br>Available strength:<br>▪ 45 mg |
| Triptorelin pamoate | Gonapeptyl (UK, EU, SA, elsewhere)<br>Decapeptyl (UK, elsewhere)<br>Triptodur (US) | Intramuscular depot injections.<br>Available strengths:<br>▪ 3.75 mg every 28 days<br>▪ 11.25 mg every 3 months<br>▪ 22.5 mg every 6 months |

Approval of these GnRH agonists for use in central precocious puberty, dosing, and schedules of administration vary between products in different countries. Consult local product information. Short-acting GnRH preparations requiring daily subcutaneous injections or multiple daily dosing nasal spray (such as nafarelin) are not recommended, due to compliance difficulty; use of these products usually is limited to patients with sterile abscesses from depot injections. Note that the doses used to treat central precocious puberty in children are substantially higher than those used in adults for other indications, such as prostate cancer and endometriosis.

GnRH: gonadotropin-releasing hormone; US: United States; CAN: Canada; EU: European Union; AU: Australia; SA: South America; UK: United Kingdom; FDA: Food and Drug Administration.

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Graphic 72979 Version 16.0

## Feminizing effects in male-to-female transgender persons

| Effect | Onset | Maximum |
|---|---|---|
| Redistribution of body fat | 3 to 6 months | 2 to 3 years |
| Decrease in muscle mass and strength | 3 to 6 months | 1 to 2 years |
| Softening of skin/decreased oiliness | 3 to 6 months | Unknown |
| Decreased sexual desire | 1 to 3 months | 3 to 6 months |
| Decreased spontaneous erections | 1 to 3 months | 3 to 6 months |
| Male sexual dysfunction | Variable | Variable |
| Breast growth | 3 to 6 months | 2 to 3 years |
| Decreased testicular volume | 3 to 6 months | 2 to 3 years |
| Decreased sperm production | Unknown | >3 years |
| Decreased terminal hair growth | 6 to 12 months | >3 years* |
| Scalp hair | Variable | —¶ |
| Voice changes | None | —Δ |

* Complete removal of male sexual hair requires electrolysis or laser treatment or both.

¶ Familial scalp hair loss may occur if estrogens are stopped.

Δ Treatment by speech pathologists for voice training is most effective.

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Graphic 54189 Version 13.0

## Masculinizing effects in female-to-male transgender persons

| Effect | Onset | Maximum |
|---|---|---|
| Skin oiliness/acne | 1 to 6 months | 1 to 2 years |
| Facial/body hair growth | 6 to 12 months | 4 to 5 years |
| Scalp hair loss | 6 to 12 months | —* |
| Increased muscle mass/strength | 6 to 12 months | 2 to 5 years |
| Fat redistribution | 1 to 6 months | 2 to 5 years |
| Cessation of menses | 1 to 6 months | —¶ |
| Clitoral enlargement | 1 to 6 months | 1 to 2 years |
| Vaginal atrophy | 1 to 6 months | 1 to 2 years |
| Deepening of voice | 6 to 12 months | 1 to 2 years |

* Prevention and treatment as recommended for biological men.

¶ Menorrhagia requires diagnosis and treatment by a gynecologist.

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Graphic 75101 Version 14.0

## Contributor Disclosures

**Johanna Olson-Kennedy, MD** Consultant/Advisory Boards: Novartis [Transgender adolescents and young adults]. All of the relevant financial relationships listed have been mitigated. **Michelle Forcier, MD, MPH** Consultant/Advisory Boards: Folx Health[Protocols, library articles, training];OutCare[LGBTQ+ health care];Planned Parenthood[Clinical services]. Other Financial Interest: Springer [Pediatric gender care (book royalties)]. All of the relevant financial relationships listed have been mitigated. **David Brent, MD** Grant/Research/Clinical Trial Support: AFSP [Suicide prevention]; NIMH [Child and adolescent psychiatry]; Once Upon a Time Foundation [Suicide prevention]; The Beckwith Institute [Healthcare grants for patient care]. Consultant/Advisory Boards: AFSP [Suicide prevention]; Healthwise [Consumer health education]; Klingenstein Third Generation Foundation [Child and adolescent mental health]. Other Financial Interest: eRT Inc [Clinical assessment, electronic self-rated version of the C-SSRS]; Guilford Press [Royalties, Depression and suicidality]. All of the relevant financial relationships listed have been mitigated. **Mitchell E Geffner, MD** Grant/Research/Clinical Trial Support: Adrenas [Congenital adrenal hyperplasia]; Diurnal [Congenital adrenal hyperplasia]; Neurocrine Biosciences [Congenital adrenal hyperplasia]; Novo Nordisk [Growth]; Spruce Biosciences [Congenital adrenal hyperplasia]. Consultant/Advisory Boards: Adrenas [Congenital adrenal hyperplasia]; Aeterna Zentaris [Growth]; Eton [Congenital adrenal hyperplasia]; Neurocrine Biosciences [Congenital adrenal hyperplasia]; Novo Nordisk [Growth]; Nutritional Growth Solutions [Growth]; Pfizer [Growth]; Spruce Biosciences [Congenital adrenal hyperplasia]. Other Financial Interest: McGraw-Hill textbook royalties [Pediatric endocrinology]. All of the relevant financial relationships listed have been mitigated. **Diane Blake, MD** No relevant financial relationship(s) with ineligible companies to disclose. **Mary M Torchia, MD** No relevant financial relationship(s) with ineligible companies to disclose.

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