

ECHO

The Gender Diversity Referral Pathway for Children

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Disclosures

- None
- I will briefly be discussing off-label use of medications

By the end of this talk you should be able to:

1

Have tools to ask about gender identity and pronoun use

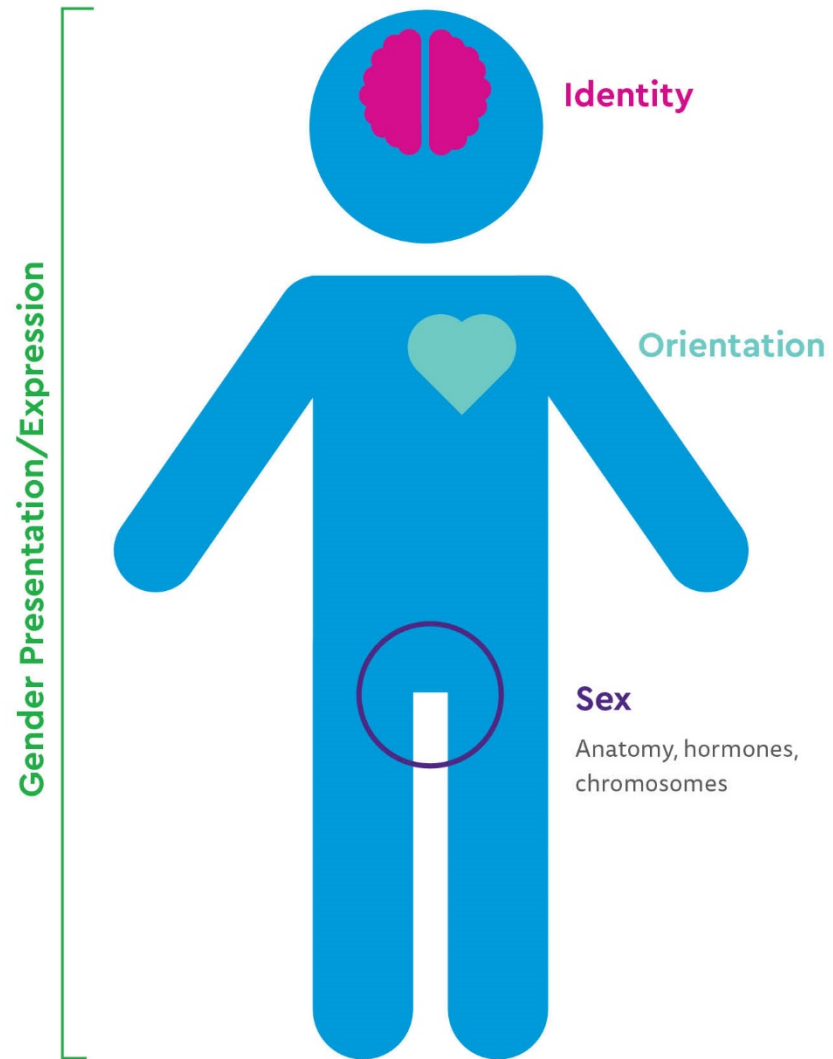
2

Understand the effects of puberty blockers & gender-affirming hormone therapy

3

Understand how guidelines are different between adults and children

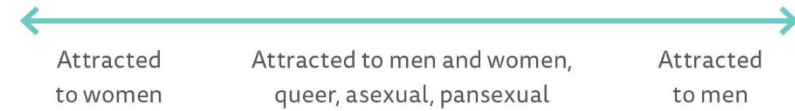
Understanding Gender



Gender Identity • *how you see yourself*



Sexual Orientation/Attraction • *who you love*



Sex Assigned at Birth • *the body parts you were born with*



Gender Presentation/Expression • *how you present yourself*



Background

- 1.8% of high school youth identify as transgender
- 1.6% are not sure
- 2017 Youth Risk Behavior Survey (YRBS, 10 states, 131,901 students)
- Prior estimates: 0.7% of youth ages 13-17 years

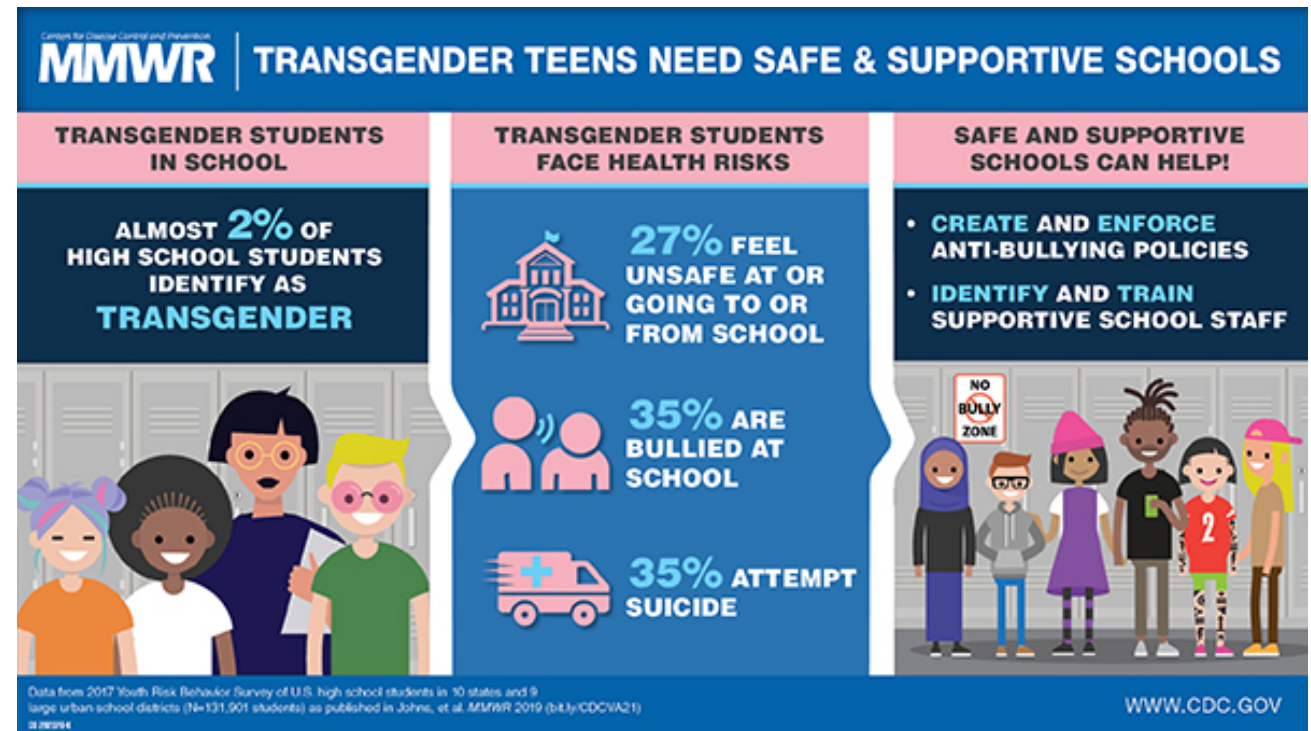
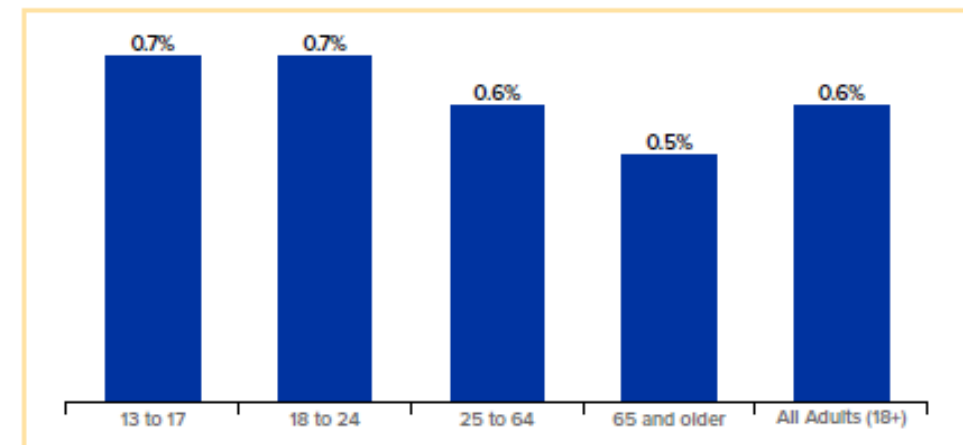
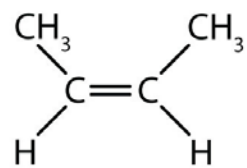
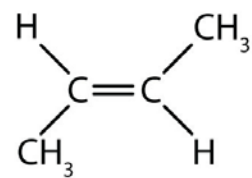


Figure 1. Percentage of Individuals Who Identify as Transgender by Age





cis-2-butene



trans-2-butene

Terminology

Name

- “Is there a name you go by other than your legal name?”
- “What name do you go by?”
- “What would you like me to call you?”

Pronouns



- “What pronouns do you use?”
- “I’d like to use the pronouns that feel best to you. What pronouns would you like me to use?”
- Normalize pronoun use: “Hello, my name is Dr. ____ I use she / her / hers pronouns.”



Gender identity

- “How do you identify your gender?”
- “What does [gender identity term] mean to you?”
- Kids: “Some kids tell me think of themselves as girls, some as boys, some as part girl and boy, or something entirely different. How do you think about yourself?”
- Teens: “There are lots of ways people think about their gender identity, how do you think of yours?”

Gender Affirmatory Language

- Avoid gendered language
 - Move away from: guys / sir / ladies
 - Try using: Everyone / folks / you all / your child / the patient/ the client
- Talk about anatomy separate from gender
 - People with a penis / uterus
 - People who menstruate / have a period
 - Avoid terms like “male anatomy” or “female reproductive organs”
- People may or may not identify as transgender; gender diversity is complex. Ask people how they identify themselves. For example, “are there any terms that you use to describe your gender identity?”
- Don’t use “transgendered” (e.g. you wouldn’t say someone is “femaed”)
- Avoid transgender as a stand-alone term. Avoid saying “the patient is a transgender” the more affirming way to say that is “the patient is a transgender woman / individual” (use transgender as an adjective not a noun)

Final tips



Be cognizant of *where* you are asking these questions



Might the location pose a safety risk to patients?

Gender Nonconformity Is Not the Same as Gender Dysphoria

Gender nonconformity refers to the extent to which a person's gender identity, role, or expression differs from the cultural norms prescribed for people of a particular sex (Institute of Medicine, 2011). *Gender dysphoria* refers to discomfort or distress that is caused by a discrepancy between a person's gender identity and that person's sex assigned at birth (and the associated gender role and/or primary and secondary sex characteristics) (Fisk, 1974; Knudson, De Cuypere, & Bockting, 2010b). Only *some* gender-nonconforming people experience gender dysphoria at *some* point in their lives.

Medical interventions for transgender youth

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POLICY STATEMENT Organizational Principles to Guide and Define the Child Health Care System
and/or Improve the Health of all Children



Ensuring Comprehensive Care and Support for Transgender and Gender- Diverse Children and Adolescents

Jason Rafferty, MD, MPH, EdM, FAAP, COMMITTEE ON PSYCHOSOCIAL ASPECTS OF CHILD AND FAMILY HEALTH,
COMMITTEE ON ADOLESCENCE, SECTION ON LESBIAN, GAY, BISEXUAL, AND TRANSGENDER HEALTH AND WELLNESS

CLINICAL PRACTICE GUIDELINE

Endocrine Treatment of Gender-Dysphoric/ Gender-Incongruent Persons: An Endocrine Society* Clinical Practice Guideline

Wylie C. Hembree,¹ Peggy T. Cohen-Kettenis,² Louis Gooren,³ Sabine E. Hannema,⁴
Walter J. Meyer,⁵ M. Hassan Murad,⁶ Stephen M. Rosenthal,⁷ Joshua D. Safer,⁸
Vin Tangpricha,⁹ and Guy G. T'Sjoen,¹⁰



Standards of Care for the Health of Transsexual, Transgender, and Gender- Nonconforming People

The World Professional Association for Transgender Health

Version 7

Guidelines/Policy Statements

Medical Interventions for Transgender Youth

Female gender identity

1. GnRH agonists to block puberty

Block male puberty changes

2. Estradiol

Induce female puberty



Male gender identity

1. GnRH agonists to block puberty

Block female puberty changes

2. Testosterone

Induce male puberty



GnRH agonists

GnRH agonists
to block puberty
aka “puberty
blockers”

Tanner 2
Generally used
age ~8-14

Male sex, female gender identity

Effects: penis/testicles stay the same size
Do not develop: body hair, facial hair, deep voice, muscle mass

Female sex, male gender identity

Effects: chest/breasts stay the same size
Do not develop: hips, periods

*Note: *exact effects depend on the puberty stage at which they are started*

Medical interventions are determined on a case-by-case basis and not everyone with a diverse gender identity receives these therapies

Gender-affirming hormone therapy

Age 14-16+

Post-pubertal

Estradiol + androgen blockade

Effects: breast development, hips, changes in fat distribution



Testosterone

Effects: deep voice, body and facial hair, increased muscle mass and strength, clitoral growth



Note: medical interventions are determined on a case-by-case basis and not everyone with a diverse gender identity receives these therapies

Estradiol

- Oral 17-beta estradiol (E2)
- Estradiol patch

TABLE 1B: EFFECTS AND EXPECTED TIME COURSE OF FEMINIZING HORMONES ^A

| Effect | Expected onset ^B | Expected maximum effect ^B |
|--|------------------------------------|--------------------------------------|
| Body fat redistribution | 3–6 months | 2–5 years |
| Decreased muscle mass/strength | 3–6 months | 1–2 years ^C |
| Softening of skin/decreased oiliness | 3–6 months | Unknown |
| Decreased libido | 1–3 months | 1–2 years |
| Decreased spontaneous erections | 1–3 months | 3–6 months |
| Male sexual dysfunction | Variable | Variable |
| Breast growth | 3–6 months | 2–3 years |
| Decreased testicular volume | 3–6 months | 2–3 years |
| Decreased sperm production | Variable | Variable |
| Thinning and slowed growth of body and facial hair | 6–12 months | > 3 years ^D |
| Male pattern baldness | No regrowth, loss stops 1–3 months | 1–2 years |

^A Adapted with permission from Hembree et al. (2009). Copyright 2009, The Endocrine Society.

^B Estimates represent published and unpublished clinical observations.

^C Significantly dependent on amount of exercise.

^D Complete removal of male facial and body hair requires electrolysis, laser treatment, or both.

Testosterone

- Testosterone cypionate or enanthate
 - IM q2 weeks or SQ weekly
- Testosterone gel
- Testosterone patch

TABLE 1A: EFFECTS AND EXPECTED TIME COURSE OF MASCULINIZING HORMONES ^A

| Effect | Expected onset ^B | Expected maximum effect ^B |
|--------------------------------|-----------------------------|--------------------------------------|
| Skin oiliness/acne | 1–6 months | 1–2 years |
| Facial/body hair growth | 3–6 months | 3–5 years |
| Scalp hair loss | >12 months ^C | Variable |
| Increased muscle mass/strength | 6–12 months | 2–5 years ^D |
| Body fat redistribution | 3–6 months | 2–5 years |
| Cessation of menses | 2–6 months | n/a |
| Clitoral enlargement | 3–6 months | 1–2 years |
| Vaginal atrophy | 3–6 months | 1–2 years |
| Deepened voice | 3–12 months | 1–2 years |

^A Adapted with permission from Hembree et al. (2009). Copyright 2009, The Endocrine Society.

^B Estimates represent published and unpublished clinical observations.

^C Highly dependent on age and inheritance; may be minimal.

^D Significantly dependent on amount of exercise.

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children

Children Are Not Just Little Adults

- “Barriers”
 - Created to protect those that cannot consent (very young, disabled, etc)
 - Only 20% of pre-pubertal children persist in the gender identity that they first used after they have reached puberty
 - Mental health letter required to make sure a child is understanding the medical terminology/procedures and decision making

Endocrine Society guidelines for GnRHa

Table 5. Criteria for Gender-Affirming Hormone Therapy for Adolescents

Adolescents are eligible for GnRH agonist treatment if:

1. A qualified MHP has confirmed that:
 - the adolescent has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed),
 - gender dysphoria worsened with the onset of puberty,
 - any coexisting psychological, medical, or social problems that could interfere with treatment (e.g., that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start treatment,
 - the adolescent has sufficient mental capacity to give informed consent to this (reversible) treatment,
2. And the adolescent:
 - has been informed of the effects and side effects of treatment (including potential loss of fertility if the individual subsequently continues with sex hormone treatment) and options to preserve fertility,
 - has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process,
3. And a pediatric endocrinologist or other clinician experienced in pubertal assessment
 - agrees with the indication for GnRH agonist treatment,
 - has confirmed that puberty has started in the adolescent (Tanner stage \geq G2/B2),
 - has confirmed that there are no medical contraindications to GnRH agonist treatment.

Introduction of gender-affirming hormones (testosterone or estradiol)

Adolescents are eligible for subsequent sex hormone treatment if:

1. A qualified MHP has confirmed:
 - the persistence of gender dysphoria,
 - any coexisting psychological, medical, or social problems that could interfere with treatment (e.g., that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start sex hormone treatment,
 - the adolescent has sufficient mental capacity (which most adolescents have by age 16 years) to estimate the consequences of this (partly) irreversible treatment, weigh the benefits and risks, and give informed consent to this (partly) irreversible treatment,
 2. And the adolescent:
 - has been informed of the (irreversible) effects and side effects of treatment (including potential loss of fertility and options to preserve fertility),
 - has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process,
 3. And a pediatric endocrinologist or other clinician experienced in pubertal induction:
 - agrees with the indication for sex hormone treatment,
 - has confirmed that there are no medical contraindications to sex hormone treatment.
-

- Age \geq 16 years
 - “We recognize that there may be compelling reasons to initiate sex hormone treatment prior to the age of 16 years in some adolescents with GD/gender incongruence, even though there are minimal published studies of gender-affirming hormone treatments administered before age 13.5-14 years.”

Practically

- Letter from a behavioral health provider
- Consent from all medical decision-makers if <18 years

Table 10. Medical Risks Associated With Sex Hormone Therapy

Transgender female: estrogen

Very high risk of adverse outcomes:

- Thromboembolic disease

Moderate risk of adverse outcomes:

- Macroprolactinoma
- Breast cancer
- Coronary artery disease
- Cerebrovascular disease
- Cholelithiasis
- Hypertriglyceridemia

Transgender male: testosterone

Very high risk of adverse outcomes:

- Erythrocytosis (hematocrit > 50%)

Moderate risk of adverse outcomes:

- Severe liver dysfunction (transaminases > threefold upper limit of normal)
 - Coronary artery disease
 - Cerebrovascular disease
 - Hypertension
 - Breast or uterine cancer
-

Table. Standardized Incidence Ratios for Acute Cardiovascular Events in Transwomen and Transmen Receiving Hormone Therapy

| Acute Cardiovascular Events | OCs (IR)* | Using Women as Reference | | Using Men as Reference | |
|-----------------------------|-----------|--------------------------|-------------------|------------------------|-------------------|
| | | ECs | SIR (95% CI) | ECs | SIR (95% CI) |
| Transwomen | | | | | |
| Stroke | 29 (127) | 12.01 | 2.42 (1.65–3.42)† | 16.08 | 1.80 (1.23–2.56)† |
| Myocardial infarction | 30 (131) | 11.38 | 2.64 (1.81–3.72)† | 38.03 | 0.79 (0.54–1.11) |
| Venous thromboembolism | 73 (320) | 13.22 | 5.52 (4.36–6.90)† | 16.04 | 4.55 (3.59–5.69)† |
| Transmen | | | | | |
| Stroke | 6 (55) | 3.49 | 1.72 (0.70–3.58) | 4.10 | 1.46 (0.59–3.04) |
| Myocardial infarction | 11 (100) | 2.98 | 3.69 (1.94–6.42)† | 10.99 | 1.00 (0.53–1.74) |
| Venous thromboembolism | 2 (18) | 4.84 | 0.41 (0.07–1.37) | 5.56 | 0.36 (0.06–1.19) |

ECs indicates expected cases; IR, incidence rate; OCs, observed cases; and SIR, standardized incidence ratio.

*Per 100 000 person-years.

†Significant finding.

Long-term effects

Nota, Circulation, 2019

Other Reversible Interventions

- Stopping Menses
 - Norethindrone acetate 5-10 mg daily
 - Oral medroxyprogesterone 5-10 mg daily
 - Medroxyprogesterone acetate depot injection q3 months
 - Etonogestrel implant
 - Levonorgestrel IUD
- Chest Binders
- Anti-androgens
- Spironolactone
 - Starting doses vary
 - Monitor serum potassium after starting
- Cyproterone acetate
 - Used in Canada & Europe
 - Higher risk of liver toxicity

Fertility

- Clear fertility implications
 - Hysterectomy/salpingo-oophorectomy
 - Orchiectomy
- Less clear
 - Gender-affirming hormone therapy

Fertility preservation

- 40-54% of transgender adults desire future parenthood (Wierckx, et al, 2012; Tornello et al, 2017, De Sutter et al, 2002)
 - Half said they wanted genetically related offspring (Tornello et al, 2017)
- Fertility preservation
 - 51% of transgender women & 38% transgender men said they would have considered sperm or oocyte cryopreservation had it been offered prior to initiation of gender-affirming hormone therapy (Wierckx, et al, 2012; De Sutter et al, 2002)
- Utilization rates are low
 - Cost, delay of gender affirming-hormone treatment, invasiveness of procedures (worsening of dysphoria)

Overview of fertility implications

- WPATH, American Society for Reproductive Medicine (ASRM) and Endocrine Society recommend fertility preservation counseling prior to starting *any* gender-affirming hormone therapy
- GnRHa administration pauses gonadal maturation
- GnRHa with later T/E2 → germ cells never fully mature
- Older individuals – cryopreservation
- Younger individuals – experimental

Masculinizing treatment



- Paucity of data, small observational case series, short durations of testosterone
- Some studies report an ovarian histological phenotype similar to PCOS, while others do not
- Two studies of AMH before and after testosterone with conflicting results
- At least some transgender men on testosterone can conceive
 - Survey of transgender men who had a live birth (Light, 2014)
 - 80% resumed menses within 6 months of T cessation
 - 84% used their own oocytes
 - 32% conceived while on testosterone
 - Over half were on testosterone for <2 years

M Moravek, *Curr Opin Obstet & Gynecol*, 2019

Pics: <https://metro.co.uk/2019/03/06/trans-man-fell-pregnant-surprise-baby-just-started-transition-8838887/>

Feminizing treatment

- Older, observational studies with inconsistent results
- Testicular histology at the time of gender-affirming surgery
 - Smaller seminiferous tubules, abnormal appearance of Sertoli & Leydig cells
 - Impaired spermatogenesis (maturation arrest)

Practically....

- We know that GnRHa in isolation are reversible
- Not much is known about T/E2 alone or with prior GnRHa

My approach

- Talk with all patients about fertility
- We don't know all the impacts of hormone therapy on fertility
- Plan as if you will be infertile
- There are lots of ways to be a parent
- T or E2 is not contraception

References

- WPATH Standards of Care, version 7 (8th version coming soon, https://www.wpath.org/media/cms/Documents/SOC%20v7/Standards%20of%20Care_V7%20Full%20Book_English.pdf)
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- childrenscolorado.org/TRUE