PEDIATRIC AND ADOLESCENT MEDICAL CARE OF GENDER DIVERSE PATIENTS

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APRIL 13, 2024

5

DISCLOSURES

- We have no financial disclosures
- All gender affirming medications are considered "off label" by the FDA but they are all FDA approved medications with research to support effectiveness and safety and guidelines for their use.

6

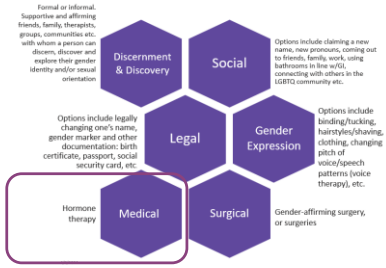
ACTIVITY OBJECTIVES

- Apply strategies to utilize gender exploration, mental health therapy and family therapy to support patients, parents/guardians, and families as they pursue gender-affirming care.
- Describe the options for gender-affirming medical and surgical care and key counseling components for consenting adolescents and parents/guardians for treatment.
- Discuss the requirements for informed consent for gender-affirming care and learn how to navigate situations when agreement to care is not present.

7

Gender-Affirming Care

People choose which, if any, option(s) will help bring them closer to a sense of gender congruence, based on their unique goals and needs.



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9

WPATH SOC 8 Recommendations:

Relevant WPATH SOC 8 recommendations: Standards of Care for the Health of Transgender and Gender Diverse People, Version 8 (tandfonline.com)

- ***6.12.f***- Adolescent has reached Tanner Stage 2 of puberty for pubertal suppression to be initiated.
- **6.6-** Health education on chest binding and genital tucking is provided, including a review of the benefits and risks.
- **6.7-** Providers consider menstrual suppression agents for adolescents experiencing gender incongruence who may not desire testosterone therapy, who desire but have not yet begun testosterone therapy, or in conjunction with testosterone therapy for breakthrough bleeding.
- **6.8**- HCP's maintain an ongoing relationship with the gender diverse and transgender adolescent and caregivers to support the adolescent in decision making throughout the duration of puberty suppression treatment, hormonal treatment, or gender-related surgery until the transition has been made to adult care.
- **6.9**- HCP's involve relevant disciplines, including mental health and medical professionals, to reach a decision about puberty suppression, hormone initiation, or gender related surgery is appropriate and remains indicated throughout the course of treatment until the transition is made to adult care.
- ***6.12.e***- The adolescent has been informed of the reproductive effects, including potential loss of fertility and available options to preserve fertility, and these have been discussed in the context of the adolescent's stage of pubertal development.
  - **6.10**- The patient is made aware of the reproductive effects including potential loss of fertility and options to preserve fertility within the context of the youth's stage of pubertal development.
  - **7.8**- Information about gender affirming medical interventions, effects of treatment on future fertility, and options for fertility preservation are provided to gender diverse children and families/caregivers when they approach puberty.

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10

Puberty

- Puberty may be a time when an acute dysphoric crisis develops as a child/teen recognizes body changes in a direction not desired, or that feel incongruent to their developing gender identity. Can lead child/teen and parents/family to seek care and support.
- **Can increase their distress and lead to risk of suicide and self-harming behaviors.**
  - Suicide is the leading cause of death among LGBTQ youth-
    - 41% suicide attempt rate and much higher incidence of self-harming behaviors than in non-LGBTQ population
- "Pronouns matter, to the point of life or death: Transgender and nonbinary youth who reported having their pronouns respected by all or most of the people in their lives attempted suicide at half the rate of those whose pronouns were disregarded."
  - The Trevor Project National Survey on LGBTQ Youth Mental Health 2020

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13

Consultation with patient and parent(s)/guardian(s)

- Discuss gender history
- Discuss goals and expectations
- Discuss family/social support system
- Assess pubertal stage
- Review medical, surgical, family, social, and mental health history
- Discuss gender-affirming care options:
  - Social transition
  - Legal transition
  - Puberty suppression therapy (if appropriate)
  - Hormone therapy (if appropriate)

14

Gender history

Diagnosis of gender incongruence and/or dysphoria

Marked incongruence between one's experienced gender and one's natal gender of at least 6 months duration as experienced by at least 2 of the following:

- Marked inconguence between one's experienced gender and one's primary and/or secondary sex characteristics (or what is expected to develop)
- A marked desire to be rid of one's primary and/or secondary sex characteristics due to the incongruence
- A strong desire for the primary and/or secondary sex characteristics of another gender
- A strong desire to be another gender
- A strong desire to be treated as another gender
- A strong conviction that one has the typical feelings and reactions of another gender

15

Mental health support and letter of support

- When is active mental health support and/or a LOS needed/should be requested to prescribe puberty suppression or hormone therapy?
  - If gender history is unclear or unsure if experiencing gender dysphoria
  - If therapeutic interventions and gender exploration are needed
  - If mental health concerns are present/co-occurring (to continue therapy and/or confirm stability)
  - If parent/family support isn't present or needs more support with/for parents and family
  - If goals include future gender-affirming surgery
  - If prescribing clinician is unable to do complete biopsychosocial assessment/diagnostic assessment needed for insurance or surgeries (may be beyond scope of practice)
  - If prescribing clinician concerned that prescribing may be clinically unsafe, a LOS may be indicated (listen to your gut) -- but not "gate keeping"

17

Discussion of goals & expectations

- Short-term goals
  - What physical changes in the short run are most important to them?
  - Do goals line up with what is feasible for puberty suppression, menstrual suppression and/or gender affirming hormone administration?
- Long-term goals
  - What physical changes to they want to have accomplished in 3-5 years? 10 years?
  - Are those goals feasible medically?
- Expectations of what puberty suppression therapy, hormone therapy, or surgery will do for them.

19

Discuss family/social support system

- Family support throughout the process is the biggest predictor of mental health and wellbeing and can reduce the risk of suicide, depression, illegal drug use and other risky behaviors.
- Partner with mental health clinician to support patient and family.
- Provide community resources and support groups to help patient and families find support.

21

Resources for Support

transforming families

RECLAIM!

gender spectrum

QUEER SPACE collective

22

Review patient history

Surgical	Medical	Mental health	Family	Social
• Previous penile or scrotal surgery • Previous breast surgery • Previous gynecological surgery	• Bone disease, low bone density • Vit D deficiency or calcium abnormality • Kidney disease • Endocrine disorders • Cardiovascular disease • Clotting disorders • Liver disease	• Co-occurring mental health concerns	• Early onset cardiovascular disease • Mental health concerns • Clotting disorders- specifically parents • Diabetes • Thyroid disease	• Nicotine use • Cannabis use • Alcohol use • Drugs use • Sexual activity: ○ Pregnancy test ○ STIs ○ PrEP

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24

Assessing pubertal stages

- ***6.12.f***- Adolescent has reached Tanner Stage 2 of puberty for pubertal suppression to be initiated.
- Discuss any concerns/dysphoria with anatomy and developing (anticipate developing) secondary sex characteristics.

Table 6. Tanner Stages of Breast Development and Male External Genitalia

The description of Tanner stages for breast development:
1. Prepubertal
2. Breast and papilla elevated as small mound; areolar diameter increased
3. Breast and areola enlarged, no contour separation
4. Areola and papilla form secondary mound
5. Mature; nipple projects, areola part of general breast contour
For penis and testes:
1. Prepubertal, testicular volume <4 mL
2. Slight enlargement of penis; enlarged scrotum, pink, texture altered, testes 4–6 mL
3. Penis longer, testes larger (8–12 mL)
4. Penis and glans larger, including increase in breadth; testes larger (12–15 mL), scrotum dark
5. Penis adult size; testicular volume > 15 ml

Adapted from Lawrence (56).

Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society* Clinical Practice Guideline | The Journal of Clinical Endocrinology & Metabolism | Oxford Academic (oup.com)

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25

Tanner staging of puberty

Assess for:
- Chest tissue/breast growth
- Public hair growth
- Menstruation

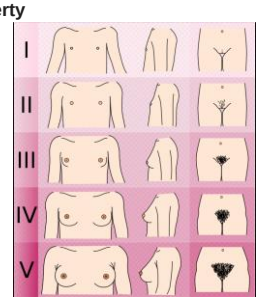

Illustration by Michał Komorniczak

Additional details of "Validity of Self-Assessment of Pubertal Maturation" available through American Academy of Pediatrics; Pediatrics. 2015;135(1):86-93. doi:10.1542/peds.2014-0793

Validity of Self-Assessment of Pubertal Maturation | Pediatrics | American Academy of Pediatrics (aap.org)

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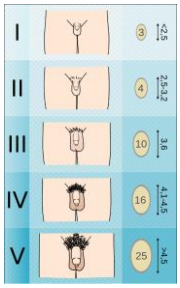
26

Tanner staging of puberty

Assess for:
- Growth of penis, scrotum, testes
- Public hair growth



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Validity of Self-Assessment of Pubertal Maturation | Pediatrics | American Academy of Pediatrics (aap.org)

Illustration by Michal Komorniczak

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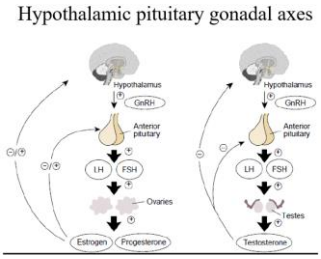
27

Puberty Suppression Therapy

- Gonadotropin-releasing hormone agonist (GnRH agonist) medication is used for puberty suppression (puberty blockers), which reduces sex hormone levels and temporarily stops the development of the secondary sex characteristics with puberty.
- Used for a long time in children with precocious puberty. Used for 20+ years to treat healthy adolescents with gender dysphoria.
- Using therapy gives time to explore gender identity and doesn't mean one must use hormone replacement therapy or have gender-affirming surgery in the future.
- Can't reverse secondary sex characteristics that have already developed.



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Puberty Suppression- benefits & risks

Benefits	Risks
Pauses the pubertal changes, and fear of ongoing future changes, that can be a source of dysphoria and pressure.	Long-term side effects on overall health and brain development are unknown.
Gives time to work with behavioral health/sexual health to explore gender identity and pros/cons of natal puberty vs hormone replacement therapy.	Side effects of the medications. Potential effects on mood (mood changes, mood swings)
Pause changes before permanent body changes/characteristics occur. May lead to fewer and less complex medical/surgical interventions in future to align the body with gender identity.	For assigned male at birth, less tissue may develop on penis and scrotum and may make future bottom surgery (i.e. penile inversion vaginoplasty) more difficult to complete (less tissue available to use for surgery).
Can stop puberty suppression at any time and body will continue through natal puberty.	Affects how body absorbs calcium and can reduce bone density. Unknown if increases risk of osteoporosis when older. (Calcium and vitamin D intake/supplement and weight-bearing exercises is important)
	Infertility if using puberty suppression then gender-affirming hormone therapy and didn't go through natal puberty.

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29

Puberty Suppression- options

Gonadotropin-releasing hormone (GnRH) agonists

- Injectables: **Lupron Depot (IM**) and **Eligard (SQ)** (typical dosage 22.5 mg every 3 months)
  - Shorter duration, so easy to stop if wanting to discontinue treatment.
  - If not given at regularly prescribed intervals, pubertal changes may still occur.
  - Usually given in clinic every 3 months (depending on prescribed dose and adjustments during course of treatment).
- Implants (in-clinic insertion procedure): **Histrelin Supprelin LA** (dosage 50 mg)
  - Histrelin Vantas implants no longer available.
  - Longer duration, so pt is not reminded as regularly of need for suppression, which can decrease dysphoria for some patients.
  - In-clinic insertion procedure placed under skin on inner side of upper arm and can stay in place for 1 year (unless removed earlier to discontinue treatment).

31

Puberty Suppression- considerations

Medication considerations:

- Very expensive (Supprelin LA $50,000+ per implant, Lupron/Eligard 22.5mg approximately $1400 per injection, Lupron 11.25mg approximately $11,700 per injection).
- Prior authorization needed through insurance.
- General recommendation is to use suppression for no longer than 2-5 years, but it may be possible to use them longer depending on clinician's recommendation.
  - Histrelin could stay in to be used for its androgen suppression effects, while also prescribing estrogen hormone therapy to achieve feminizing secondary sex changes.

Once suppression therapy ends, either natal puberty or hormone therapy begins (estrogen or testosterone therapy). The body can't avoid puberty entirely or not have any hormones in it.- Will not develop pubertal changes at the same time as same age peers (though the range for the rate/timing of pubertal development is notoriously wide)

32

Puberty Suppression- considerations

- Monitor growth (height, weight) and puberty changes every 3-6 months
  - If taken during growth spurt, may have slightly shorter final adult height than would have otherwise
- Monitor labs every 6-12 months
  - CBC, CMP, LH, FSH, Estradiol, Testosterone, Vit D
- Monitor bone density with Dexa scan every 1-2 years

- This medication isn't contraception and doesn't protect from sexually transmitted diseases.

34

Puberty Suppression- body effects/changes

Assigned Female at birth	Assigned Male at Birth
Stops menses (or won't start). Decreases fertility/ability to get pregnant while using medication. Fertility returns if progresses through natal puberty after stopping suppression.	Stops growth of testes, scrotum, and penis. Decreases fertility/ability to get someone pregnant while using medication. Fertility returns if progresses through natal puberty after stopping medication.
Stops chest tissue/breast growth (or won't start).	Decreases or stops nocturnal emissions (or won't start)
Growth/height slower than if going through puberty.	Growth/height slower than if going through puberty
May experience vaginal dryness and reduced sex drive.	Causes erectile dysfunction, fewer spontaneous erections, reduced sex drive
Won't develop softer skin, wider hips, and/or more fat on hips.	Stops further increase of facial and body hair growth (or won't start)
	Stops further development of facial structures (increased brow ridge, Adam's apple, angular appearance) and body structure (broader shoulders, more muscle development)

35

Puberty Suppression- side effects

- Puberty changes/symptoms can continue in the first 4 weeks after starting treatment (i.e. irregular bleeding).
- Mood changes and mood swings
- Headaches, hot flashes (sweating, warmth or redness in face, neck, arms, upper chest) and night sweats, figure, muscle pain and weakness, dizziness
- Weight gain
- GI upset- nausea, vomiting, diarrhea
- Risk of allergic reaction; pain, soreness, bruising at injection/implant site; risk of infection with any injection or implant. Risk of implant migrating from insertion site.
- Uncommon risks:
  - Increased risk seizures
  - Cardiovascular effects (risk in cisgender males using medication for prostate cancer. Risk in healthy adolescents is unknown.)
  - Pseudotumor Cerebri (idiopathic intracranial hypertension)

36

Menstrual suppression

Multiple options which can be used together or separately

- Depo Provera – potential for weight gain, mood issues
- High dose oral progestins – Medroxyprogesterone 20-30 mg daily or Norethindrone 5-10 mg daily – same side effects
- Nexplanon can work enough for some patients but usually not amenorrheic
- Mirena IUD can work but lead in of several months spotting and can be associated with cramping. Disadvantage of needing to insert either in the office or the operating room, and not a good choice if uterus is too small.
- Continuous OCPs/NuvaRing but may be dysphoric and/or induce more feminizing changes if early in puberty
- Leuprolide Acetate (DepoLupron)
- Elagolix – GnRH antagonist, no data in young patients
- General Approaches to Medical Management of Menstrual Suppression | ACOG

38

DESIRE FOR NO HORMONES

Increasingly, there are people who express the desire to avoid having either masculinizing or feminizing hormones in their bodies.

Counseling points:

- Puberty cannot be avoided entirely
- Hormones affect more than secondary sex characteristics: bone health, growth, brain development, cardiovascular health
- Patients can use time while on suppression therapy to consider which hormones will be the least dysphoric for them.

39

HORMONE THERAPY BENEFITS AND RISKS

Benefits	Risks
Individualized therapy based on patient's goals for gender alignment. Better align body with gender identity.	Long-term risk are not fully known.
Increased positive mental health outcomes and quality of life.	Potential effects on mood (mood changes, mood swings) and worsen mental health conditions (anxiety, depression, bipolar disorder, schizophrenia, ADHD).
Decreased risk of anti-LGBTQ violence, by helping to "pass" as individual's identified gender.	Affects how body absorbs calcium and can reduce bone density. Unknown if increases risk of osteoporosis when older.
Close to zero regret: lower than for knee replacement.	Decreased fertility during treatment. Infertility if using puberty suppression then gender-affirming hormone therapy and didn't go through natal puberty.

41

HORMONE THERAPY – GOALS AND EXPECTATIONS

Gender-affirming hormone therapy is used to develop the secondary sex characteristics that are in line with the patients' gender identity.

- Changes take time and happen at different rates.
- The rate of change depends on an individual's body, and the medication's route and dose, though higher doses do not necessarily correlate with faster changes.
- Some changes are reversible, some are semi-permanent, and others are permanent.
- The affects achieved through hormones are dependent on an individual's genes. Ex: some people grow lots of facial hair in a day, for others it can take months; some people develop large breasts, others' breasts are smaller.

42

MASCULINIZING HORMONE THERAPY OPTIONS

- Testosterone options:
  - Transdermal: Gels of varying strengths
  - Injection (IM or subQ), usually weekly
    - Testosterone cypionate
    - Testosterone enanthate
    - Xyosted SQ injection pen
  - Long acting:
    - Aveed testosterone undecanoate injection (at PN MPLS Gender Services)
    - Testopel testosterone pellets (at PN MPLS Gender Services)
  - Oral
    - Jatenzo, Tlando and Kyzatrex are all testosterone undecanoate with absorption via lymphatics, avoiding the liver. Not interchangeable

43

MASCULINIZING HORMONE THERAPY OPTIONS

- Typically, visits are every 8-12 weeks for the first year, then visits are less often
- Each visit clinical and laboratory response is assessed
- Assessment of impact of medication and other adjunctive measures on gender dysphoria is done as part of assessing clinical response.

45

TESTOSTERONE THERAPY PHYSICAL EFFECTS

Timeline is typically 1-12 months and can take up to 1-5 years for maximal changes to occur.

Potentially permanent body changes:

- growth of facial hair and body hair,
- decreased scalp hair (including male pattern baldness),
- deepening of voice,
- clitoromegaly (clitoral enlargement),
- menstrual suppression/cessation of menses,
- infertility.

Timeline for Effects of Masculinizing Hormone Therapy

Effect	Onset of changes	Maximum effect reached at:	Reversibility
Acne, oily skin	1 to 6 months	1 to 2 years	High
Fat redistribution	1 to 6 months	2 to 5 years	Moderate
Menstrual suppression, cessation of menses	1 to 6 months, most often closer to 6 months		High*
Clitoral enlargement	1 to 6 months	1 to 2 years	Low
Vaginal atrophy	1 to 6 months	1 to 2 years	Low
Deepening of the voice	2 to 6 months	1 to 2 years	Considered permanent
Increase in muscle mass and strength	6 to 12 months	2 to 5 years	Moderate
Facial/body hair growth	6 to 12 months	4 to 5 years	Low
Scalp hair loss**	6 to 12 months	Dependent on genetic predisposition	Low

47

TESTOSTERONE THERAPY POTENTIAL RISKS AND SIDE-EFFECTS

Decreased estrogen

- Hot flashes, headaches, mood swings
- Vaginal dryness (can last years)
- Urinary frequency

Testosterone

- Acne
- Polycythemia and blood clots
- Mood swings, quicker to anger
- Increased depression, increased anxiety
- Mental health instability (especially with bipolar, schizophrenia, and other mood disorders)
- Worsening ADHD symptoms (including difficult to focus, concentrate)
- Increased sex drive (evens out over time)
- Elevated blood pressure, elevated cholesterol, diabetes.
- Irregular vaginal bleeding
  - Too high testosterone, metabolizes to estrogen
  - Too low testosterone, may NOT suppress ovulation

48

ESTROGEN AND ANDROGEN BLOCKERS - OPTIONS

- Estrogen options:
  - Pills
  - Patches
  - Injections (IM or subQ), usually weekly
    - Estradiol valerate
    - Estradiol cypionate
- Androgen blockers options:
  - Spironolactone
  - Finasteride
  - Dutasteride

Progesterone is not typically used in adolescents, since it is not used until 1-2 years after starting estrogen to promote breast growth.

Use of Bicalutamide pills for androgen blockers **not recommended**

- Clinician visits and lab monitoring typically every 3 months for first year of initiation then 1 to 2 times per year once levels are stable.
- This medication isn't contraception and doesn't protect from sexually transmitted diseases.

50

ESTROGEN AND ANTI-ANDROGEN PHYSICAL EFFECTS

Timeline for body changes is typically 3-6 months after starting therapy and can take up to 2-3 years for maximal changes to occur.

Potentially permanent body changes:

- breast growth
- decrease testicular volume
- decreased sperm production
- infertility

Timeline for Effects of Feminizing Therapy

Effect	Onset of changes	Maximum effect reached at	Reversibility
Decreased spontaneous erections	1 to 3 months	3 to 6 months	High
Erectile dysfunction	Variable	Variable	High
Decreased libido	1 to 3 months	3 to 6 months	High
Decrease in muscle mass and strength	3 to 6 months	1 to 2 years	High
Redistribution of body fat	3 to 6 months	2 to 3 years	High
Softening of skin/decreased oiliness	3 to 6 months	Unknown	High
Decreased testicular volume	3 to 6 months	2 to 3 years	Unknown
Decreased sperm production	Unknown	> 3 years	Unknown**
Breast growth	3 to 6 months	2 to 3 years	Considered permanent
Decreased terminal hair growth	6 to 12 months	> 3 years*	High, except for electrolysis or laser treatment
Scalp hair	Variable	Variable; familial scalp hair loss pattern may occur	Low
Voice changes	Only achieved through voice training by speech pathologists		High

52

ESTROGEN AND ANTI-ANDROGEN POTENTIAL RISKS AND SIDE-EFFECTS

- **Estrogen**
  - Hot flashes, headaches, mood swings (usually in the first few weeks of use)
  - Weight Gain
  - Elevated blood pressure
  - Elevated triglycerides, cholesterol
  - Blood clots – worst with oral administration
  - Gallbladder disease with oral administration
  - Unknown about decreased bone density, breast cancer
  - Prolactinoma
  - Mental health instability, worsening mood issues, increased anxiety, depression
  - Infertility

54

ESTROGEN AND ANTI-ANDROGEN POTENTIAL RISKS AND SIDE-EFFECTS

- Anti-Androgens
  - Spironolactone
    - Lower blood pressure
    - Dizziness
    - Frequent urination
    - Elevated potassium and/or elevated creatinine
    - Infertility
  - Finasteride, Dutasteride
    - Depression
    - Infertility
    - Rarely, liver disease

55

FERTILITY PRESERVATION DISCUSSION

- Tools available to facilitate a family discussion – Trans Youth and Family/Parent Questionaires that can be a starting point for discussion at home and then brought in for more in depth conversation with mental health and/or medical clinicians
- More than one visit discussion
- Storing actual testicular or ovarian tissue via cryopreservation is possible at Mayo Children's Program as part of a study
- Storing sperm or ova may be very dysphoric for the patient

59

FERTILITY PRESERVATION DISCUSSION

Assigned male at birth

- Best to store sperm before starting gender affirming medication. Sperm is not mature enough for storage in pre-pubertal males.
- Fertility may return off estrogen and anti-androgens

Assigned female at birth

- Freezing ova technology is improving, is possible before starting gender affirming testosterone if menarche has occurred
- Fertility usually returns off testosterone

DECREASED FERTILITY DOES NOT IMPLY THAT CROSS GENDER HORMONES ARE CONTRACEPTION!

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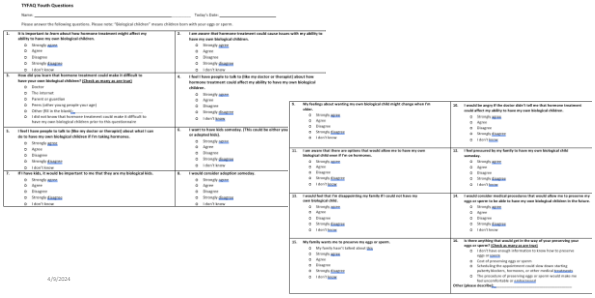
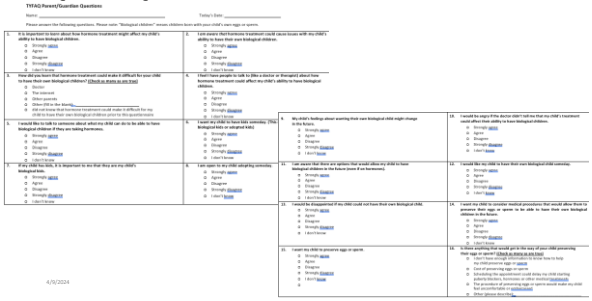
60

TYFAQ Youth Questions



61

TYFAQ Parent Questions



62

TYFAQ Comparison Chart

63

FERTILITY EFFECTS OF PUBERTY SUPPRESSION AND/OR GENDER AFFIRMING HORMONE THERAPY

Therapy	Assigned female at birth	Assigned male at birth
Puberty suppression	Suppresses menses	Stops growth of testes, scrotum, penis Decreases/stops nocturnal emissions Causes erectile dysfunction, decreases spontaneous erections Decreases libido
Stops suppression and proceeds through natal puberty	Menses resume and reproductive organs fully develop	Sperm production resumes and reproductive organs fully develop
Stops suppression and proceeds to hormone therapy	Infertility, because reproductive organs didn't fully develop	Infertility, because reproductive organs didn't fully develop
Hormone therapy	Suppresses menses Suppresses ovulation (not always, so pregnancy still possible. Testosterone is category X teratogenic medication so can cause birth defects) Increases libido (may level out over time)	Decreases sperm production (though could still get someone pregnant) Decreases testicular volume Causes erectile dysfunction, decreases spontaneous erections Decreases libido

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NAVIGATING DISCUSSIONS WHEN PARENTS/GUARDIANS DON'T AGREE TO CARE

- Clinicians can and should:
  - Educate all parties on what puberty suppression and/or gender affirming hormones will and will not do for and to the patient, and options available to address concerns
  - Listen to goals and expectations of each party
  - Is there anyplace where agreement can be found to build consensus?
  - Offer family therapy, individual therapy resources
  - Offer resources for support groups to help with family education around gender diversity

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HealthPartners and Park Nicollet Gender Services

If you work in the system, there is a referral you can place to Gender Services and we will get the patient in with the appropriate clinician(s)

If you don't want to place a referral or don't work in the system, call 952-993-8052 and we will get the patient in with the appropriate clinician(s)

68

69