Gender non-conforming children & youth

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• I have no financial conflicts with commercial interest companies.
• I do intend to discuss off-label use of products and/or devices and will inform you of such uses.
Objectives

• After this presentation, I hope you:
  – Know terms relevant to care for transgender people
  – Know the basics of what transgender people need from all healthcare providers
  – How & when medical transition should happen for children & adolescents
Let's start where I started: DSDs (disorders of sexual development/intersex)

• Male and female are not as clear as we would like them to be (and assume they are!)
  – XX can = male (xx male), XY can = female (turner, swyer, CAIS)
  – Females can have testes (CAIS), males can have ovarian tissue (true hermaphrodite)
  – A male can have a uterus (PMD) and a female a phallus (CAH)

• The only organ that conclusively determines gender is the brain

• Therefore, the only way a doctor can know for sure is to ask the patient
**LGBTQ Language: Sex**

- **Sex (Assigned at birth)**
  - Typically based on appearance of physical anatomy
  (ASAB= Assigned Sex At Birth)
  - Can include:
    - Chromosomes,
    - Reproductive organs
    - Internal genitalia
    - External genitalia
    - etc

- **Intersex**

- **Female**

- **Male**
LGBTQ Language: Gender

- **Gender Expression**
  - Clothing, mannerisms, voice

- **Gender Norms**
  - Social and cultural expectation of expression

- **Gender Identity**
  - Personal sense as a gendered being

- **Cisgender**
  - Man
  - Woman

- **Transgender**
  - Transman
  - Transwoman
  - Non-binary

Slide courtesy of K. Imborek, MD
Transgender Terms

- **Transman/Transboy**: Female To Male
- **Transwoman/Transgirl**: Male To Female

**Transition**
- Process of moving from one gender to another
- May no longer identify as trans* after transitioning to affirmed gender
- “Pre-op” and “post-op” are outdated and should be avoided
Non-Binary

- Third gender
- Genderqueer
- Gender fluid
- Pronouns:
  - She, her, hers
  - He, him, his
  - They, them, theirs
  - Ze, zir, zirs
  - Ne, nem, nirs

Slide courtesy of K. Imborek, MD
A little history!

I love medical history!
A trans* timeline (modern medicine only)

- **1910** Magnus Hirschfeld introduces the term "transvestites",
  - To distinguish from people who are homosexual.
- **1920s-30s** sex reassignment surgery first developed in Germany
- **1929** estrogen was isolated
- **1935** testosterone was isolated & synthesized
- **1942** FDA approves estrogen therapy (Premarin)
- **1950s** testosterone enanthate (the first non-toxic testosterone) becomes available
- **1953** The physician Harry Benjamin introduces the term "transsexuals",
  - To distinguish transgender people from transvestites.
- **1955** The American psychologist John Money introduces the distinction between "sex" and "gender".
- **1965** The word transgender was first used medically (by Dr. John F. Oliven)
  - However- transgender was given its meaning by Virginia Prince (a trans woman) in the 1970s
- **1966** The term 'gender identity' is first used
Some historic trans people

- **1917 USA: Dr. Alan L. Hart, (1890-1962) (expert in TB)**
  - undergoes hysterectomy and gonadectomy.
  - He (successfully) lived the rest of his life as a man.

- **1951 USA: Christine Jorgensen**
  - first transgender woman in the US to be widely known for having sex reassignment surgery (in 1951)
  - also treated with estrogen
But what about children?

• **1980s-90s** Prof. Dr. Peggy T. Cohen-Kettenis established the first treatment center for transgender children and adolescents (in the Netherlands)
  – Her team is the source of nearly all scientific evidence on transgender children
  – We all use their protocol

• **2007** Dr. Norman Spack established the first US treatment center for trans children and adolescents
What do doctors need to know to care for trans* patients?
Transgender Healthcare: Medically Necessary?

- American Medical Association
- American Psychiatric Association
- American Psychological Association
- American Academy of Family Physicians
- National Association of Social Workers
- National Commission on Correctional Health Care
- World Professional Association for Transgender Health
- American Public Health Association
- American College of Obstetricians and Gynecologists
- Pediatric Endocrine Society
- Endocrine Society
- American Academy of Pediatrics
Name and Pronouns

• The **most important thing** when caring for trans patients:

• Use their **preferred** name
  – “what do you like to be called”

• Use their preferred **pronouns**
  – “what pronouns do you prefer”
    – (pronouns **are not required to match gender identity** - pronouns are public, gender identity is private)

• If the parent doesn’t use their name or pronouns: you **should still use their preferred name and pronouns**

• If you make a mistake: apologize and move on
• Emily is a 17 yo gender queer person, sex assigned at birth male. They complain of abdominal pain that has affected them for the past month. Emily states that they have tried Tums without relief of their pain.

• Jordan is a 16 yo gender queer person, sex assigned at birth female. Ze complains of abdominal pain that has affected zir for the past month. Jordan states that ze has tried Tums without relief of zirs pain.
Concerns from Trans Patients

• Access to care
• Respect
  – Use their preferred name and pronouns
  – don’t ask about or look at their genitals unless you need to in regards to their specific concern
• Cost
• Provider knowledge/comfort
Barriers specific to kids

- **Parents!**
  - In Iowa, there is no “emancipated minor” for the purposes of trans care
  - Consent of at least one guardian (with at least 50% custody) is required to undergo therapy

- **Access!**
  - There are not enough providers who will see pediatric patients

- **Cost**
  - Not as much of a problem as for adults, actually . . .
Gender Inclusive Tips

Instead of:

- Mr, Mrs, Ms, Miss, sir, ma’am
- She, he or
- Asking for their “real” or “legal” name
- Hoping the patient is used to being called the wrong pronoun/name
- Gossiping or joking with other office staff

Use:

- Preferred name
- “The patient” or they
- “Could your chart be listed under a different name”
- “I apologize for using the wrong pronoun/name earlier”
- Maintain confidentiality as per HIPPA guidelines for all patients
Why treat trans* children?

*very similar to why we treat adults

Note: Children know their gender as young as 2 years of age!
prevalence

• Historically: thought to be 0.1% of the population

• In a population-based survey of 80,929 9th and 11th graders
  – 2.7% reported being trans or gender non-conforming
    • Did *not* differ between urban and rural
    • More common in Native American and low income teens

• Other reasonable studies have reported 1-4% population prevalence

Rider et al. Pediatric 2018
Depression!

- Rates of depression are 2-3 times higher in transgender youth vs. non-transgender peers\(^1\)
  - Data suggest this is caused by discrimination, peer rejection and lack of social support\(^2\)

- The best predictor of positive psychological outcomes is parental support\(^2\)

- Transgender children that undergo a social transition have rates of depression comparable to non-transgender children\(^3\)

Suicide

- 61% of high-school age transgender/GNC youth report suicidal ideation\(^1\)
  - (20% of cisgender youth)
- 31% have attempted suicide\(^1\)
  - (7% of cisgender youth)
- 45% of trans 16-25 year olds who don’t have support attempt suicide\(^2\)

- "The minute these kids even know they’re [getting treated], their suicidal thoughts melt away."\(^2\)

\(^1\)Eisenberg J Adolesc Health 2018 \(^2\)Spack Boston Children’s hospital
• 2x as many trans and GNC youth report poor health as cisgender peers

• Trans and GNC youth have higher rates of:
  – Binge drinking, substance use, high-risk sexual behaviors and being victims of bullying

Rider et al. Pediatrics 2018
• Above is Corey Maison (14 yo)
• Right is Jazz Jennings (15 yo)
So how do we treat trans* children & youth?
Not- "reparative or conversion" therapy

- Therapy with the goal to change a person’s gender identity to become more congruent with sex assigned at birth
  - has been attempted in the past without success\(^1\), particularly in the long term\(^2\).
  - Such treatment is not ethical and amounts to torture
  - the American Psychological Association, the American Psychiatric Association and the American Academy of Pediatrics all reject this form of therapy

\(^1\)Gelder & Marks, 1969; Greenson, 1964; \(^2\)Cohen-Kettenis & Kuiper, 1984; Pauly, 1965;
First- diagnosis of gender dysphoria

- To be made by a mental health professional
- For peds- that person should be pediatric/adolescent trained
  - Establish that GID/transgender is the diagnosis
  - rule out body dysmorphic disorder
  - diagnose and treat any other psychiatric disorders
    - Other psychiatric disorders, including schizophrenia do not preclude transition, but they need to be managed
Pubertal suppression with GnRH analogs is the preferred method

- starting at tanner 2
3rd- Cross-sex steroids

• Recommended regimen is different than for adults!
  – We are essentially inducing puberty much as we would in any hypogonadal child

• Start at 15-16 years*

• IM/sub q T or oral/patch estradiol

• Dose escalation every 4-6 months starting at low doses
  – Starting low & titrating gives better physical outcomes (breast/voice/bone structure)

• GnRH treatment is (ideally) continued until gonadectomy or doses are high enough to suppress HPH axis
  – If can’t get GnRH, can use depo provera, spironolactone, bicalutamide depending
• Mastectomy can be done before age 18
  – Eligible at 16 years

• Other procedures need to 18 or older

• Note:
  – Vaginoplasty is harder if they transitioned younger as it typically utilizes penis skin

• You will get an update on surgical procedures tomorrow, so stay tuned!
What if we just wait?

• withholding puberty suppression and subsequent feminizing or masculinizing hormone therapy is **not a neutral option** for adolescents
  – functioning in later life can be compromised by
    • development of irreversible secondary sex characteristics
    • years spent experiencing intense gender dysphoria.
  – contributes to an appearance that can provoke abuse and stigmatization
    • the level of gender-related abuse is strongly associated with
      the degree of psychiatric distress during adolescence¹

¹Nuttbrock et al., 2010
Differences between children and adolescents

- Gender dysphoria occurring prior to puberty does **not** inevitably continue into adulthood.
  - Gender dysphoria persists in 6-23% of AMAB children\(^1\) and 12-27% of AFAB children\(^2\).

- In contrast, the persistence of gender dysphoria into adulthood is higher for adolescents with essentially all continuing \(^4\).

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\(^1\)Green, 1987; Money & Russo, 1979; \(^2\)Drummond, Bradley, Peterson-Badali, & Zucker, 2008; Wallien & Cohen-Kettenis, 2008; \(^3\)Zucker & Bradley, 1995; Zuger, 1984; \(^4\) de Vries, Steensma, Doreleijers, & Cohen-Kettenis, 2010; \(^5\)Zucker, 2004; \(^6\)Cohen-Kettenis & Pfäf in, 2003
So what do we do with pre-pubertal children?

- **Recommended:**
  - **Social transition**
    - Dress in preferred clothes
    - Preferred hairstyle
    - Preferred toys
    - Preferred name
  - **Support for affirming activities**
    - Girl/boy scouts, dance, sports, etc

- **How can you tell who will persist?**
  - We don’t have great ways yet, but there are clues:
    - Repudiation of genitalia
    - Statements of identity “I *am* a girl” or “I am a girl in a boy’s body” rather than “I *want* to be a girl” or “I *wish* I was a girl”
Outcomes

Does it work? Does it help?
What are the risks?
Risks

- therapy is overall safe
- cancer risk is not higher than expected
- thromboembolic risk
  - significant with ethinyl estradiol preparations
  - Lower with the current oral and patch 17-beta estradiol
  - There is increased risk for thromboembolic complications compared to cis women
- testosterone may worsen the cardiovascular profile of transmen, but only in comparison with cisgender women, not cisgender men
- the risk of puberty suppression and cross-sex hormones is low in contrast with the high rate of suicide in untreated transgender individuals (~40%)

Nota et al. Circulation 2019
Outcomes of gender transition

• in adults
  – hormone replacement therapy and gender affirming surgery
    • improve gender dysphoria
    • Improve quality of life
    • Reduce suicide
  – However:
    • persistence of psychiatric comorbidity
    • Still some death from suicide
Outcomes are improved when transition starts in adolescence

- Those who are treated in childhood have much lower rates of suicide and psychopathology than trans patients who present as adults\(^1\)

- Long term study of 55 transgender adolescents who underwent puberty suppression and cross-sex hormones followed by gender affirming surgery in early adulthood\(^2\)
  - Complete resolution of gender dysphoria
  - Psychological outcomes that were similar or better than non-transgender, age-matched young adults
  - None of these patients regretted their decision to transition

- Better cosmetic outcomes
  - If treated starting at tanner 2
    - Height appropriate to affirmed gender
    - Bone structure of affirmed gender
  - Very different physical appearance than transition as an adult, especially for transfemales

\(^1\)de Vries, A.L.et al. 2011, \(^2\)Cohen-Kettenis et al., 2011; Delemarre-van de Waal & Cohen-Kettenis, 2006
Fertility

• GnRH agonists – if started in early puberty (Tanner stage II-III), lack of development

• Testosterone induces amenorrhea in postmenarchal transmales;
  – number of cases of unplanned pregnancy while on treatment
  – planned pregnancy and uneventful child birth

• Estrogen treatment may lead to sterility
• **Ask** preferred name and pronouns
• **Use** preferred name and pronouns

• Medical transition **can** (& I think should!) start once there is clear evidence of puberty
  – Tanner 2!
• LGBTQ clinic
  – Dr. Nicole Nisly
  – Dr. Katie Imborek

• University of Iowa Adolescent Medicine
  – Dr. Michael Colburn

• Elizabeth Graf PA-C Ob/Gyn; reproductive endocrinology
Thank you!

• Questions?
Trans*

- Incongruity between sex assigned at birth and gender identity

- May not conform to societal norms for:
  - Gender expression
  - Gender norms
  - Gender identity
How do you know someone’s **gender**?

A. Chromosomes
B. Ask them
C. Look at their genitals
D. Look at how they dress
How do you know someone’s **sex**?
A. Karyotype them (XX or XY)
B. Examine their genitals
C. Assay hormones to determine if they have ovaries or testes
D. Pull their birth record
E. Ask them
F. All of the above, depending on the situation
G. None of the above
What else is different with transition in adolescence?

• Surgery is different
  – MTF need less ancillary surgeries
  – But more difficult vaginoplasty

• Fertility
  – Early GnRH agonists decrease fertility above estrogen and testosterone alone


Definitions

• **Sex-**
  Physical- chromosomes, gonads, internal reproductive organs and external genitalia
  – Not always binary
  – Not always in consistent

• **Gender-**
  a non-binary construct that allows for a range of *gender identities* and that a person’s *gender identity* may not align with sex assigned at birth\(^1\)

• **Gender identity** –
  innermost concept of self as male, female, a blend of both or neither
  • the only thing that determines gender is the *brain*

\(^1\)American Psychological Association
Definitions

• **Sex Assigned at birth**- just what it sounds like!
  – AFAB = “assigned female at birth”
  – AMAB = “assigned male at birth”

• **Gender role**- behaviors, attitudes and personality traits that assign masculinity/femininity culturally

• **Gender nonconformity**- the extent to which a person’s gender identity, role, or expression differs from the cultural norms

• **Gender dysphoria**- discomfort or distress that is caused by a discrepancy between a person’s gender identity and that person’s sex assigned at birth\(^1\)

\(^1\)DSM-5
Definitions

- **Transgender*** - a person who identifies as or desires to be accepted as a gender different to the assigned gender at birth. Includes persons whose gender identity does not conform to conventional gender roles of either male or female.

- **Cisgender** - a person who identifies as the same gender as their assigned gender at birth.

- **MTF** - male to female - person transitioning from male to female.

- **FTM** - female to male – person transitioning from female to male.

- *There exist many more terms that gender non-conforming or transgender persons may use to describe themselves - those should always be used as per the person’s preference.*
Genital surgery

• Criteria
  – 18 years of age
  – Successful use of cross-sex hormones for 12 months
  – Successful RLE for 12 months
  – If MHP requests- regularly participated in mental health care
  – Understand the costs, risks, complications, hospital stay and rehabilitation required.
  – Mental health has improved and gender identity is consolidating
• Penectomy/Gonadectomy
• Vaginoplasty
  – This is **harder if they transitioned younger** as it typically utilizes penis skin

• Ancillary surgery
  – Voice change surgery not recommended
  – Breast augmentation should be delayed for at least 2 years of estrogen therapy for max natural growth
  – Facial surgery
    • These are **typically not needed** if transitioned in childhood or early teenage years
Surgery- FTM

- Less satisfactory than MTF
- Neopenis --multistage and very expensive
- Metaidoioplasty
  - Allows for voiding while standing
- Oophrectomy
- Vaginectomy
- Complete hysterectomy
  - After a few years of androgen therapy
- Mastectomy- if transitioned in childhood/adolescence may have already been done/ not needed
Objectives

• After this presentation, I hope you:

  – Have a basic understanding of the guidelines for care of the transgender child

  – Understand the implications of gender transition in childhood for an adult patient and their care provider

  – Be aware of the resources at the University of Iowa for gender-nonconforming children
• “The big difference is that the adults lived an entire life in another role before seeking treatment, and in many cases it was not by choice. People acquire attachments—family, friends, a job—and any number of those things can be lifted away from them because of their decision to be something they always felt they were.”

• “The under-21-year-olds are just not the same population as the adults. They can’t identify with the adults, but they can identify with Lenore from “Orange is the New Black” because she’s a young woman, so she clearly went through a phase not unlike their own. They look at transgender adults coming out and say, “What were you waiting for”?”
"reparative or conversion" therapy

- therapy with the intention of changing one’s gender identity or sexual orientation
- the American Psychological Association, the American Psychiatric Association and the American Academy of Pediatrics, reject this form of therapy
Treatment is different in children

- Fully reversible interventions.
  - GnRH analogues “blockers”
  - progestins (most commonly medroxyprogesterone)
  - other medications (such as spironolactone)
  - Continuous oral contraceptives (or depot medroxyprogesterone) may be used to suppress menses.

- Partially reversible interventions.
  - hormone therapy to masculinize or feminize the body.

- Irreversible interventions
  - surgical procedures.
Endocrine therapy for FTM

• Similar to treatment of male hypogonadism
• Parenteral or transdermal preparations are acceptable
  – Goal is normal testosterone range (320-1000 ng/dl)
  – Parenteral testosterone enanthate/cypionate 100-200mg im q 2 weeks or 50% weekly
  – Transdermal
    • Gel 1% 2.5-10 g/d
    • Patch 2.5-7.5 mg/d
• Can use GnRH to stop menses and reduce estradiol levels
Effects of treatment

- Increased muscle mass
- Decreased fat mass
- Increased facial hair, acne, libido
- Male pattern baldness
- Clitoromegaly
- Decreased fertility
- Deepening of voice
- May stop menses
  - May take a few months, may require high doses, may need progesterone or ablation to fully achieve this
Endocrine therapy for MTF

- Oral: estradiol 2.0-6.0 mg/d
- Transdermal: estradiol patch 0.1-0.4 mg twice weekly
- Parenteral estradiol valerate or cypionate 5-20 mg im q 2 weeks, or 2-10 mg im q week
- Optional (to reduce androgens to female levels)
  - Antiandrogens- Spironolactone 100-200 mg/d
  - GnRH agonist 3.75 mg sc monthly
Effects of therapy

• Redistribution of body fat
• Decreased muscle mass and strength
• Softening of skin, decreased oil
• Decreased libido/ spontaneous erections
• Male sexual dysfunction
• Breast growth (maximum effect at 2 years)
• Decreased testicle volume
• Decreased sperm production
• Decreased terminal hair (No complete removal)
• NO increase in scalp hair
• NO voice change (speech pathology)
• Peter Daniolos MD- psychiatry
• William Davis MD- Ob/Gyn, reproductive endocrinology
• Ginny Ryan MD- Ob/Gyn, reproductive endocrinology
• Elizabeth Graf PA-C- Ob/Gyn, reproductive endocrinology
• there seems to be a higher prevalence of autistic spectrum disorders in clinically referred, gender dysphoric adolescents than in the general adolescent population (de Vries et al., 2010).
• Treatment not to begin prior to puberty
  – There is a significant rate of remission of GID after onset of puberty (~75%)

• However
  – There is significant psychological distress caused by puberty in adolescents with GID disorder.
  – Reduced dysphoria and better psychological and physical outcomes are reported starting younger in puberty
“I met [Alfred Kinsey] . . . he asked my advice in [a] case . . . . This very effeminate boy wanted, as he said, to become a girl, and his mother supported him in this. Kinsey had never seen a case like this, and it was new even for me. It went well beyond what was by then recognized transvestism. The concept of transsexualism did not yet exist. . . . However, the boy received "female" hormones that "had a calming effect". He then travelled to Germany, where he underwent partial surgery. After that, I unfortunately lost contact with him, and thus I do not know what ultimately became of the case."

“One must understand the main problem of transsexuals. In English, it is properly named "gender dysphoria", i.e. a discrepancy between anatomy and sexual self-identification.”
  – “It does not follow that one should perform surgery in every case.”
  – “Many may also manage without surgery as long as they are being treated with hormones and can wear the clothing of the desired (more precisely: truly felt) sex.”

From an interview with Dr. Benjamin on his 100th birthday 1/12/1985- translated from the German
Let’s start where I started:
Disorders of Sexual Development

• Current term: disorder of sexual development (DSD)

• previous term: intersex disorders
  – Still acceptable for use, may become recommended term again

• Old term: (perjorative!) hermaphrodite
  – People who are intersex may refer to themselves using this term, medical professionals should not!