Care of gender non-conforming children & adolescents

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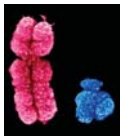
I have no financial relationships to disclose.

Terminology: Sex

- **Sex assigned at birth**
  - Based on appearance of external genitalia
- Chromosomal sex
- Gonadal sex
- Sex of internal reproductive structures
- Sex of external reproductive structures (genitalia)

- **Male**
- **Female**
- **Intersex**



Slide courtesy of K. Imborek, MD

Differences of sexual development (DSDs)

- DSD = disorder 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 ($_{\text{xx male}}$), XY can = female ($_{\text{turner,swyer,CAIS}}$)
  - Females can have testes ($_{\text{CAIS}}$), males can have ovarian tissue ($_{\text{true hermaphrodite}}$)
  - A male can have a uterus ($_{\text{PMD}}$) and a female a phallus ($_{\text{CAH}}$)
- 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

Terminology- gender

- Gender
  - Usually when we speak of gender we mean **gender identity**
- Gender (identity)-innermost concept of self as male, female, a blend of both or neither- *A* person's *gender identity* may not align with sex assigned at birth[1]
  - Gender role- behaviors, attitudes and personality traits that assign masculinity/femininity culturally
  - Gender expression- ways in which a person communicates gender identity to others
  - 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[2]

[1]American Psychological Association, [2] DSM-V

Terminology- gender identities

- Transgender- a person who identifies as or desires to be accepted as a gender different to the sex assigned at birth.
  - Also may include 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 sex assigned at birth
- People can also identify as:
  - Agender- do not identify with any gender
  - Gender fluid- the gender they identify most with varies over situations/time
  - Genderqueer- identifying neither as male or female
  - Third gender
  - Etc.

Human brain- development

- Sex differences in the brain are present before adolescence
  - sex differences were observed at the age of 7 in total brain volume, gray and white matter volume[1]
- But- puberty is the period of greatest divergence in human brains[2]
  - changes in cortical thickness are related to testosterone levels[3]
    - polymorphisms of the androgen receptor moderate the effect of testosterone on brain volumes in boys[5] .
  - estradiol is related to gray matter development in girls[4]
  - The rate of increase of testosterone during puberty was more important to the development of a gendered personality than the amount of testosterone[9]
- Hypothalamic INAH3 ("human SDN-POA") region is differentiated by gender[6]
  - It also differs between gay and straight men[7]

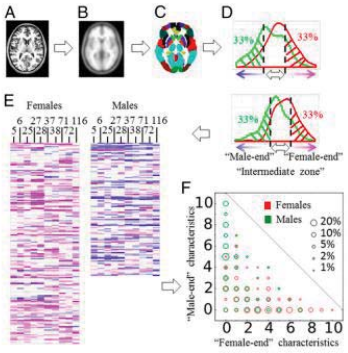
[1]Giedd et al., 2012, [2]Lenroot and Giedd 2010[3]Nguyen et al., 2012, [4]Peper et al., 2009, [5]Paus et al., 2010
[6]Allen et al 1989, [7]LeVay 1991, [9]McHale et al 2009

The transgender brain

- Untreated trans people performed in the direction of their affirmed gender on gender on sex-specific tests in some studies[1,2], but not others[3]
- MRI data
  - 24 MTF transgender individuals who had not yet begun hormone were mostly similar to control men- However, right putamen (BSTc) in these subjects, was more feminine[4]
  - a separate study of 24 MTF individuals observed thicker cortices compared with 24 age-matched control men in a number of regions. [5]
  - Yokota et al found in both FTM and MTF the corpus callosum shape more closely resembled controls of the affirmed gender rather than birth gender.
- Post mortem data (complicated by cross-sex steroid therapy):
  - In 1995, Zhou et al found that the size and the number of neurons in the BSTc of 6 MTF estrogen-treated transgender individuals was similar to control females
    - Chung et al. (2002) showed that the sex difference in the BSTc, the nucleus that was found to differ between transsexuals and non-transsexuals (Swaab and Garcia-Falgueras, 2009) became significant only in adulthood.
  - 2008, Garcia-Falgueras and Swaab reported that INAH3 (the "human SDN") volume and neuron number in 11 MTF transgender persons was in the female range

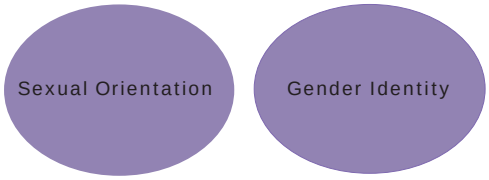
[1]Cohen-Kettenis 1998, [2]Van Goozen 2002, [3]Haraldsen 2003, [4]Garcia-Falgueras and Swaab 2009, Garcia- Falgueras and Swaab 2012[5]

Extensive overlap in "male" and "female" brains



Joel D, PNAS 2015

A word on:
Sexual Orientation & Gender Identity



How do we best care for our gender non-conforming patients?

The most important thing: Name and Pronouns

- The most important thing when caring for ANY 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

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
- Providers often tell transgender patients "I don't know how to care for you" or "I am not an expert"
  - Transgender patients are used to educating providers, but they shouldn't have to
  - They should be able to "just be a patient"

Gender Inclusive Tips

Instead of:	Use:
• Mr, Mrs, Ms, Miss, sir, ma'am	• Preferred name
• She, he or it	• "The patient" or they
• Asking for their "real" or "legal" name	• "Could your chart be listed under a different name"
• Hoping the patient is used to being called the wrong pronoun/name	• "I apologize for using the wrong pronoun/name earlier"
• Gossiping or joking with other clinic staff	• Maintain confidentiality as per HIPPA guidelines for all patients

Gender non-conformity is more common than we thought

- Historically thought to be 0.1% of the population
- In a population-based survey of 80,929 9th and 10th 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
- Available data likely underestimates prevalence

Rider et al. Pediatric 2018

Transgender Healthcare is Medically Necessary

An incomplete list of medical societies which have formally endorsed transgender care as **medically necessary** healthcare:

- 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

Why is it necessary?- 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]

[1]Reisner, S.L., et al 2015; [2]Budge, S.L. et al 2013; [3]Olson, K.R., et al 2016

This is Corey Maison- she has shared her story publicly to help other trans* people

The "real" reason- 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]

[1]Eisenberg J Adolesc Health 2018 [2] Spack Boston Children's hospital

So how do we (medically) treat trans* children?

First- not everyone who is gender colorful needs *medical* treatment

- Children ≠ adolescents
- Gender dysphoria during childhood does not inevitably continue into adulthood.
  - Historical data: Gender dysphoria persists in 6-23% of AMAB children[1] and 12- 27% of AFAB children[2]
    - AMAB children in these studies were more likely to identify as gay men in adulthood than as transgender[3]
- In contrast, essentially all adolescents continue to experience gender dysphoria into adulthood [4]

[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;

What not to do: "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[1,2], particularly in the long term[3,4].
  - 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; [2]Greenson, 1964; [3]Cohen-Kettenis & Kuiper, 1984; [4]Pauly, 1965;

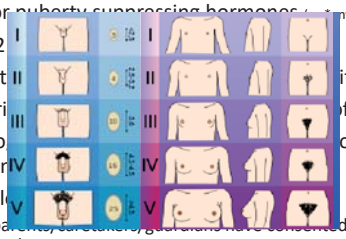
Do: First- diagnose gender dysphoria

- To be made by a mental health professional
- For peds- that person should be pediatric/adolescent trained
  - Establish that gender dysphoria 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

2nd- "Blockers"

Criteria for puberty suppressing hormones (…ny* medical therapy)

- Tanner 2
- Long last…ity/dysphoria
- Dysphori…f puberty
- Psycholo…ould interfere with treatmen
- The adol…
  - And pa…d and are supportive if required



3rd -Cross-sex steroids (estrogen & testosterone)

- 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 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

*the guidelines do not explicitly state an actual age recommendation, rather they state "in some countries 16 year olds are legal adults for medical decision-making"- and rather recommend shared decision making between the adolescent, family and the treatment team- from the WPATH guidelines – standards of care 7th edition

4th- Surgery?

- Mastectomy can be done before age 18
  - Eligible at 16 years
- For other procedures need to 18 or older
  - Many females will want vaginoplasty at some point
  - Many males do not elect phalloplasty at this time, but may want hysterectomy

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, trauma and likelihood of being a victim of homicide
    - the level of gender-related abuse is strongly associated with the degree of psychiatric distress during adolescence[1]
    - homicide is a leading cause of death in teen and adult transwomen of color, and a major risk to transwomen of all ages

[1]Nuttbrock et al., 2010,

Outcomes- does it work? Is it safe?

Is it safe?

- 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[1]
- testosterone may worsen the cardiovascular profile of transmen, but only in comparison with cisgender women, not cisgender men[1]
- the risk of puberty suppression and cross-sex hormones is low in contrast with the **high rate of suicide in untreated transgender individuals (~40%)**

[1]Nota et al. Circulation 2019

What about 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

Does it work- yes it does!

- Those who are treated in childhood have much lower rates of suicide and psychopathology than trans patients who present as adults[1]
- And much better cosmetic outcomes
  - If treated starting at tanner 2
    - Height appropriate to affirmed gender
    - Bone structure of affirmed gender
  - Very different appearance than transition as an adult, especially for transfemales (this saves lives)

[1]Cohen-Kettenis et al., 2011; Delemarre-van de Waal & Cohen-Kettenis, 2006

To sum up-

- Ask the patient's preferred name
- Use the patient's preferred name
  - Enter the preferred name into epic if it has not been entered previously
- Ask the patient's preferred pronouns
- Use the patient's preferred pronouns

- Don't ask about genitals unless you need to

University of Iowa LGBTQ care

- LGBTQ clinic
  - Dr. Nicole Nisly (IM)
  - Dr. Katie Imborek (FP)
  - Dr. Emad Abou-Arab (FP)
  - Dr. Lauren Kanner(ped endo)
  - Dr. Akhila Ramakrishna (ped endo)
  - Me (ped endo)
  - Michelle Miller (pharmD)
- University of Iowa Adolescent Medicine
  - Dr. Michael Colburn
- reproductive endocrinology/ Ob/Gyn
  - Elizabeth Graf PA-C
  - Dr. Miriam Murray
- Urology
  - Amy Pearlman
  - Brad A. Erickson
- Plastic Surgery
  - Talintope Akinboyi, MD, MSc
  - Kristopher Day, MD