CREATING A SPACE FOR TRANSGENDER CARE IN THE CLINIC

NANCY SOKKARY MD FACOG
PEDIATRIC AND ADOLESCENT GYNECOLOGY
CREATING A SPACE FOR TRANSGENDER CARE

- No conflicts of interest of Financial Disclosures
- Nexplanon Trainer
CREATING A SPACE FOR TRANSGENDER CARE

- The Barriers
- The Team
- The Training
- The Clinic
THE BARRIERS

- Lack of centers offering service to transgender adolescent
  - Provider
    - Training
    - Fear
  - Lack of support
- Lack of awareness among patients/families
- Fear of healthcare system
- High Cost
  - Leuprolide acetate $500-1000/month


THE TEAM

Provider
- Pediatric Endocrinology
- Pediatric Urology
- Medical Ethicists
- Behavioral Health Providers
- Pediatric and Adolescent Gynecology
- Adolescent Medicine
- General Pediatrics
- Primary Care Providers
- Social Workers
- Nutritionists

Staff
- Front Desk
- Nursing
- Medical Assistants
- Laboratory Technicians
- Imaging

Tishelman A, et al. 2015
THE TEAM

Education
- Residency
- Medical students
  - Individuals
  - Faculty
  - Curriculum

Community
- LGBTQ Interest Groups
  - Local and National
- DPH
THE TRAINING

- Who?
  - Everyone: front desk, nurses, medical assistants, providers, behavioral health specialist, laboratory technicians, radiology staff
  - Medical students and residents*

- How?
  - Local trainers
  - Traveling trainers
  - On-line modules
  - National Conferences

THE TRAINING: LOCAL

http://www.lgbtcenters.org/Centers/find-a-center.aspx
THE TRAINING: NATIONAL

http://transhealth.ucsf.edu/video/story.html

- http://fenwayfocus.org/2016/02/introducing-transtalks-a-transgender-health-online-training-video-series/
- http://prh.org/teen-reproductive-health/arshdp-explained/
  - Access to curriculum, modules, powerpoint
- WPATH/USPATH conference
  - Global Education Initiative
CARING FOR TRANSGENDER ADOLESCENT PATIENTS

Part 1: Initial Evaluation and Primary Care Perspective
Part 2: Ongoing Management, Hormones, Primary Care
“Create Gender Affirming Office”

Cultural Humility

First encounter

- Waiting room
  - Gender neutral and/or LGBTQ art and brochures*
  - Visible non-discrimination policy
  - Visible confidentiality policy
  - Gender neutral bathroom

- Front desk staff
  - No surprises
    - Scheduling
  - Default should be treatment like any other patient
- Training
THE CLINIC

- Intake form
  - Trained professional can do intake over the phone
  - Computer generated intake
  - “2 step approach”
    - What is your gender identity?
    - What sex were you assigned at birth?
  - Preferred name
  - Preferred pronoun

http://transhealth.ucsf.edu/trans?page=guidelines-clinic-environment

Tate CC, Ledbetter JN, Youssef CP. A two-question method for assessing gender categories in the social and medical sciences. J Sex Res. 2012 Sep 18;1-10

Sherer I. 2015.
THE CLINIC:

- Packet
  - Natal sex, gender, preferred pronoun, preferred name
  - Release of information for behavioral health provider
  - Consent for puberty blockers
  - Consent for cross sex hormone therapy
  - Follow-up

- Transgender hormone guide
  - Speak with behavioral health
  - Risks
  - Follow-up
  - Labs/Anthropomorphic measures
I hereby authorize:  

[Name/If Facility]  

Address  

[To release the indicated information from the records of:]  

[Client Name]  

[Address]  

[Date of Birth]  

[SSN]  

INFORMATION TO BE RELEASED TO:  

☐ History & Physical  

☐ Discharge Summary  

☐ Operative Reports  

☐ Pathology Reports  

☐ Lab/Xray Reports  

☐ Complete Record  

[Attn: ANDERSON HEALTH CENTER]  

[Other PH (478)633-1710 FAX (478)633-7476]  

[This information is to be released for the purpose of:]  

________________________________________________________________________  

I understand that I may withdraw this authorization with written notice except to the extent that action has been taken based on my consent.  

[Date]  

[Signed]  

[Patient, or if minor, Parent or Guardian]  

I hereby specify that this authorization to release information extends to cover release of information related to HIV-III testing; the result(s) of testing, counseling, and/or treatment of AIDS, AIDS Related Complex (ARC), or AIDS related conditions.  

[Patient, or if minor, Parent or Guardian]  

I hereby specify that this authorization to release information extends to cover release of information related to psychiatric and/or drug and alcohol abuse treatment information.  

[Patient, or if minor, Parent or Guardian]  

Disclosure of these records and information by the recipient is prohibited except when implied in the purpose of this disclosure.  

This authorization is not valid if presented more than 90 days after date signed.
<table>
<thead>
<tr>
<th>E. My signature below constitutes my acknowledgment of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td>▶ My medical provider has discussed with me the nature and purpose of hormone therapy; the benefits and risks, including the risk that hormone therapy may not accomplish the desired outcome, the possible or likely consequences of hormone therapy, and all feasible alternative diagnostic or treatment options</td>
</tr>
<tr>
<td>▶ I have read and understood the above information regarding the hormone therapy, and accept the risks involved</td>
</tr>
<tr>
<td>▶ I have met with a provider for education and support regarding hormone therapy</td>
</tr>
<tr>
<td>▶ I have reviewed a list of community services and resources for people of transgender experience</td>
</tr>
<tr>
<td>▶ I have had sufficient opportunity to discuss my condition and treatment with the medical provider, nursing staff, and/or other staff, and all of my questions have been answered to my satisfaction</td>
</tr>
<tr>
<td>▶ I believe I have adequate knowledge on which to base an informed consent to the provision of hormone therapy</td>
</tr>
<tr>
<td>▶ I authorize and give my informed consent to the provision of hormone therapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Signature of Client:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Legal Name of Client (Printed):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Signature of Witness:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of Witness (Printed):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical Provider’s Name:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>
FOLLOW-UP

- **Follow-up GnRh Analog**
  - Q 3 months
    - Ht, wt, sitting ht, Tanner stage
    - LH, FSH, Estradiol, Testosterone
  - Annually
    - BUN/CRT, LFT, lipids, glucose, insulin, HgbA1c
    - Bone Age
    - DEXA

- **Follow-up Cross-sex**
  - Q 3 months
    - Ht, wt, sitting ht, Tanner stages
  - Annually
    - Bun/Crt, LFT, lipids, HgbA1c
    - Bone Age
    - DEXA


Hembree, 2009
- ACA Section 1557
  - Prohibits denial of health coverage based on gender

- Human Rights Campaign: Finding Insurance for Transgender-Related Healthcare
  - [http://www.hrc.org/resources/finding-insurance-for-transgender-related-healthcare](http://www.hrc.org/resources/finding-insurance-for-transgender-related-healthcare)
  - Some Medicaid programs, provide for transition-related care. See your state Medicaid program for details

- Providing Transition related healthcare have very low cost and utilization
  - Benefit Employers and Employees


DON’T FORGET REFERENCE STI IN TRANS

- Talk to patient in private
- Routine Sexually Transmitted Infection screening
- Contraception counseling
- Patient’s natal anatomy
  - Torsion
  - Adnexal mass
  - PID
  - Pregnancy
    - Ectopic
    - Spontaneous abortion


- [http://transbodies.com](http://transbodies.com) - resource for patients

  - SOC for Primary and Gender Affirming Care for Transgender and Gender non-Binary People

- [www.transequality.org](http://www.transequality.org)
  - Name change, medicare, school, travel

- [www.transgenderlawcenter.org/issues/health](http://www.transgenderlawcenter.org/issues/health)
  - Name change
Navigating Transgender Adolescent Medicine: Emotional Aspects of Medical and Reproductive Treatment Among Transgender Youth

Angela K. Lawson, Ph.D.

Northwestern University
Chicago, IL
Disclosures

- Nothing to Disclose
Learning Objectives

At the conclusion of this presentation, participants should be able to:

1. Have increased sensitivity to the psychological issues surrounding transgender youth who present for medical treatment and treatment which would impair their fertility.

2. Understand the unique treatment-related psychological issues that may arise in the course of medical and fertility preservation treatment with transgender youth.

3. Be able to more confidently discuss issues related to fertility and fertility preservation with transgender patients.
Overview

I. Psychological Needs/Concerns of Transgender Youth

II. Transgender Individuals Desire For Parenthood

III. Emotional Aspects of Family Building
People are Diverse and “Transgender” is an Adjective

The Genderbread Person

by www.ItsPronouncedMetrosexual.com

**Gender Identity**

- **Woman**
- **Genderqueer**
- **Man**

Gender identity is how you, in your head, think about yourself. It’s the chemistry that composes you (e.g., hormonal levels) and how you interpret what that means.

**Gender Expression**

- **Feminine**
- **Androgynous**
- **Masculine**

Gender expression is how you demonstrate your gender (based on traditional gender roles) through the ways you act, dress, behave, and interact.

**Biological Sex**

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

Biological sex refers to the objectively measurable organs, hormones, and chromosomes. 
Female = vagina, ovaries, XX chromosomes; male = penis, testes, XY chromosomes; 
intersex = a combination of the two.

**Sexual Orientation**

- **Heterosexual**
- **Bisexual**
- **Homosexual**

Sexual orientation is who you are physically, spiritually, and emotionally attracted to, based on their sex/gender in relation to your own.
Gender Development

- Evidence of gender non-conformity as early as 2yo
  - Mean 8.3 yrs ± 4.5 (n = 96 youth)
  - Pediatricians may be first contact for families

- Persistence of gender non-conformity into adolescence/adulthood associated with gender dysphoria.
  - 2% - 27%

- Onset of puberty may result in gender-related stress

- No consistent developmental trajectory
  - Regardless, shouldn’t say “it’s just a phase”

Guss et al., 2015; Vance et al., 2014
Barriers to Transgender Patient Care

• Despite increasing number of multidisciplinary clinics in U.S. and patients presenting for medical care...

• Reluctance to disclose to health care provider
  – Social stigma
  – Cultural prejudice
  – Harassment/discrimination
    • All leading to delay/avoid medical care
    • Unsupervised hormone use 29%-63%
    • 1 in 5 reported avoiding emergency room visit
    • Increased risk of not following medical advice

Guss et al., 2015; Roberts et al., 2014; Smalley et al., 2016
Barriers to Transgender Patient Care

- National Transgender Discrimination Survey (2010) >6K participants
  - 19% refused care because of gender identity
  - 28% verbally harassed
  - 2% assaulted while attempting to receive medical care

Roberts et al., 2014; Shires et al, 2015
Psychological Needs of Transgender Patients

• Anxiety/depression
  – 2-3x greater risk than general population (44% depression, 33% anxiety)
  – 92.3% (n = 73 transgender youth) with a past/present dx of MDD, GAD, PTSD, BPD (Nahata, et al., 2017)

• Suicidality
  – 41%-60% transgender individuals attempted v. 2%-4.6% general population

• Lower academic performance

• Substance abuse

• Family/Social Conflict
  – Homelessness, decreased use of condoms, increased distress, violence
  – Increased risk of bullying, harassment and assault at school

Cicero et al., 2016; Guss et al., 2015; Roberts et al., 2014; Safer et al., 2016; Smalley et al., 2016; Vance et al., 2014
Family Building:

An Often Undiscussed Need
Family Building is Diverse
Family Building is Harder for LGBTQ Individuals/Couples

• **Biological Differences for transgender patients/couples:**
  – Conception requires third party
    • Grief over loss of privacy and one partner’s genetic link
    • More expensive
    • More decisions
      • Third party (known vs. agency/sperm bank)
      • Whose gametes or body
      • Disclosure
      • Treatment at home or in clinic
      • Attorneys
      • Etc.

Black et al, 2014; Goldberg 2010; Greenfeld 2011
Societal Differences in Family Building

- **Social Challenges**
  - Treatment in heteronormative cisgender world
    - Not a social expectation
    - Possible rejection from family/friends
    - Stereotypes of transgender individuals as incompetent parents
    - Societal stigma (invalidation of their relationship and child)
      - Double disenfranchisement

Bergstrom-Lynch, 2012; Black et al, 2014; Goldberg, 2010; Tuazon-McCheyne, 2010
Legal Differences in Family Building

- Depends on biological sex of a couple and marriage laws
  - In the U.S. no federal parenting law for same-(biological) sex couples
Social Similarities in Family Building

The Kids are Alright

• No additional risk to children of LGBTQ children as compared to cisgender heterosexual parents.
  – Includes: health, emotional well-being, coping, learning, academic, etc.

• No negative impact on the gender and sexual development of children.

• > 74 other studies confirm this!


Desire for Parenthood
Transgender Men and Women’s Desire for Parenthood

- The majority of transgender men and women are of reproductive age at the time of transition.

- Many transgender men and women are interested in fertility preservation.
  - Transgender women
    - 51% would freeze sperm or at least consider it if counseled
    - Mean age for those who freeze is 28yo (range = 20-45)
  - Transgender men
    - ~40% would consider freezing eggs
    - 54% want children
    - No research on interest in ovarian tissue cryopreservation

De Sutter et al, 2002; Light, A.D. et al., 2014; T'Sjoen, G. et al., 2013; Wierckx et al, 2012a; Wierckx et al, 2012b
Transgender Men and Women’s Desire for Parenthood

But.....

- N= 73 adolescents (50 transgender males, 23 transgender females)
- EMR review at specialty clinic
  - Median age at first endocrinology visit = 15.2 (range 9-18)
  - Median age at puberty blockers = 15.0 (range 9-18)
  - Median age at cross-sex hormone therapy = 16.0 (range = 14-18)
  - 98.6% with documented FPC
- 2 attempted FP (both biologically male)
- 45.2% planned to adopt
  - 21.9% planned to be child-free
  - 8.2% cost as a barrier
  - 1.4% discomfort with masturbation
  - 1.4% don’t want to delay hormone treatment

Chen et al., 2017; Nahata et al., 2017
Transgender Men and Women’s Desire for Parenthood

- What’s going on between adolescence and adulthood?
  - Different expectations about future family building or desire?
  - Sample differences?
  - Focus on medical treatment?
    - Desire to begin exploring relationships and discuss fertility later?
    - Dysphoria too overwhelming to engage in decision making?
  - Concerns related to stigma, societal expectations, harassment, etc?

- Effect of hormone exposure on future fertility?
  - Time to return of fertility can range from 3-6 months, some may experience permanent infertility, or require fertility treatment

Caanen et al., 2015; Light, 2014; Nahata et al., 2017
Disparities in Counseling for Fertility Preservation

• Little research

• Disparities likely exist

• Psychological consequences
  – Regret
  – Anger
  – Sadness
Emotional Aspects of Future Family Building Transgender Individuals/Couples
Emotional Aspects of Family Building: Transgender Couples

• Whose sperm and eggs?

• Biological sex of the partners

• Fertility preservation prior to hormone or surgical intervention?

• Stopping of hormones and subsequent egg retrieval or sperm
  – Risks changes to physical appearance as male or female gender
  – Onset of menses
  – Dysphoria with masturbation, vaginal exams, etc.
Emotional Aspects of Family Building: Transgender Couples

• **Who will carry the pregnancy?**
  – Gestational surrogacy vs. transgender male pregnancy

• Costs as a barrier to agency gestational surrogacy

• Increase in gender dysphoria with transgender male pregnancy
  • Feminization of appearance
  • Vaginal exams
  • Barrier to treatment and/or risk for postpartum depression.

Light et al., 2014; T'Sjoen, G., Van Caenegem, E., & Wierckx, K., 2013.
Emotional Aspects of Family Building: Transgender Couples

- Transgender male pregnancy
Emotional Aspects of Family Building: Transgender Couples

• **Who will carry the pregnancy?**

• *Transgender women report sadness that they are unable to be pregnant*

• Survey of N = 48 transgender male pregnancies
  – Mean age at conception = 28 (SD = 6.8)
  – 61% previously used testosterone
  – 88% used autologous oocytes
  – 68% planned pregnancies; 12% used ART
  – “I looked at it as something to endure to have a child”
  – Feelings of isolation

Light et al., 2014; T'Sjoen, G., Van Caenegem, E., & Wierckx, K., 2013.
Equitable Referral and Access to Family Building

• Training regarding transgender patient needs is warranted.

• All patient’s undergoing potentially fertility impairing treatment should be offered FP.

• Counseling by a MHP is warranted at the time of FP referral.
Conclusions
Conclusions

• Transgender youth navigate a series of complex barriers to obtain appropriate medical care, to protect their fertility and eventually to conceive.

• Transgender individuals have likely experienced harassment and discrimination in healthcare and social settings.

• As a result, psychological distress is common among transgender youth.

• Healthcare professionals should not provide disparate care.

• Psychological counseling should be offered to transgender patients and their families.
Conclusion

• Don’t tell your patient “it’s a phase”
• ...Or anything else that fails to take into consideration the great emotional investment it took for them to disclose their identity.
Biology of Gender

NASPAG Annual Meeting
April 2017

Selma Feldman Witchel, MD
Children’s Hospital of Pittsburgh of UPMC
Gendered society
During pregnancy, what are you having???
Newborn sex assigned by appearance of external genital structures
But.....

What happens when external genitalia are ambiguous?
Consult the pediatric endocrinologist to evaluate for a disorder of sex development
Gender and Pediatric Endocrinology

Patients with disorders of sex development

- Ambiguous genitalia
- Congenital adrenal hyperplasia
- Gonadal dysgenesis
- Complete androgen insensitivity

DSD
Gender dysphoria is defined as distress caused by the incongruence between one’s expressed or experienced (affirmed) gender and the gender assigned at birth based on external genital structures.

Data suggest that transgender youth are at a higher risk than their non-transgender peers for negative health outcomes and health risk behaviors, including:

- Substance use
- Depression
- Suicidality
- Anxiety
- Sexual/physical abuse
- STDs
- Social isolation
- Homelessness

## Demographics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Transgender Youth (N=50)</th>
<th>Non-Trans Youth (N=215)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>17.6 (1.66)</td>
<td>17.0 (1.36)</td>
<td></td>
</tr>
<tr>
<td>Proportion Biological Female</td>
<td>142 (65%)</td>
<td>35 (17%)</td>
<td></td>
</tr>
</tbody>
</table>

## Outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Transgender Youth (N=50)</th>
<th>Non-Trans Youth (N=215)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gay-related victimization</td>
<td>0.82 (.72) **</td>
<td>0.26 (.37)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender-related victimization</td>
<td>0.71 (.72) **</td>
<td>0.12 (.32)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CESD Depression Score</td>
<td>19.2 (9.1) **</td>
<td>11.5 (11.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SCARED Anxiety Score</td>
<td>27.2 (15.4) **</td>
<td>19.2 (12.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Rosenberg Self Esteem Scale</td>
<td>3.4 (1.09) **</td>
<td>4.6 (1.28)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoke Cigarettes Past 6 Mo</td>
<td>14 (28%)*</td>
<td>34 (16%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>5+ Drinks in One Sitting Past 6 Mo</td>
<td>17 (34%)*</td>
<td>37(17%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Sex with Someone First Met Past 6 Mo</td>
<td>11 (22%)*</td>
<td>25 (11%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Notes: *Analysis sample size varies across outcomes using listwise deletion. **Mean and Standard Deviation

Supported by NIH R21 DA037958 PIs: Michael P. Marshal, Ph.D. & Deena Chisolm, Ph.D. Co-Is: Selma Witchel, MD & Elizabeth Miller, MD.
Humans have been fascinated by sex development

**Hippocrates:** Both men and women emit “seeds”. Union of the stronger seeds in a favorable environment resulted in male infant.

**Aristotle:** Male and female are opposite poles. Only males emit “seed”. The semen determines the form of the embryo and is the driving force towards maleness, whereas the female provides the environment for embryonic development.

Aristotle [translated by Peck AL]: Generation of Animals (Heinemann, London 1979)
• The womb is cold and dry in temperament (testicles are hot and dry).

• The womb is divided into 7 cells with 3 cells on right, 3 cells on left, and 1 cell in the middle.

• Males develop in the cells on the right.

• Females develop in the cells on the left

• The middle cell is reserved for hermaphrodites.

This theory combined the right-left and hot-cold polarities of Greek medicine, the numerological beliefs about the number 7, and provided a simple explanation for multiple births and sex determination.
In 19th century, increased focus on “categorization” and “cataloguing”

“What was one to do with a person who seemed to be neither or both male and female?

How could one distinguish between “normal” from “homosexual” relations if one could not clearly divide all the parties into males and females?”

Everyone, including every doubtful person, had to have one permanent “true” sex
Two-spirit people (Berdashe) is a modern term used by some native North Americans to describe gender-variant individuals in their communities. Male berdashes combined the social roles assigned to both genders. They could dress like women, combine male and female dress, or alternate modes of dress. Their occupational role permitted a combination of male and female work to achieve exceptional productivity.

Callender et al. Current Anthropology 1983; 24:
Does exposure to androgens during critical stages of fetal or postnatal development influence biology and behavior?
Multiple factors influence gonadal development.

To investigate the effects of sex hormones and the Y chromosome on human behavior, development, gender identity, and sexual orientation, individuals with DSDs have been considered to be “experiments of nature” especially females with CAH.
Outcomes

- Internal and external genital structures
- Sexual behavior
- Aggression
- Infant care
- Spatial abilities
- Play/toy preferences
- Gender identity
Girls with CAH are more likely to play with “boy-typical toys” and engage in “male typical” leisure activities and occupations.

9/14 studies show that girls with CAH have increased masculine identity whereas other 5 studies found no differences.

In general, more severely virilized girls show greatest degree of masculinization.

Does socialization influence gender-related behavior?
Increased Cross-Gender Identification Independent of Gender Role Behavior in Girls with CAH

4 groups (age range 4-12 yrs)
Girls with CAH
Control girls
Boys with CAH
Control boys

Measures
Gender Identity Interview for Children
Parent Report Gender Identity Questionnaire
Parent Interview for Cross-Gender Identification

Results
Younger children gave more ambiguous responses. However, ambiguous responses were more common among girls with CAH.

More girls with CAH showed preferences for cross-gender roles, games, and peers

Pasterski V, et al. Arch Sex Behav. 2015;44:1363
Increased Cross-Gender Identification Independent of Gender Role Behavior in Girls with CAH

High scores indicate cross-gender

Pasterski V, et al. Arch Sex Behav. 2015;44:1363
Androgen exposure seems to play a decisive role in the development of gender-typical behavior in children with DSD conditions.

Most women with CAH are heterosexual.

For women with CAH, physical change from female to male is relatively uncommon, but occurs more frequently than among the general population.

Hormone exposure, surgery, & environment may influence behavior, gender identity, and sexual activity.

Berenbaum & Meyer-Bahlburg. Horm Metab Res 2015;47:361
Prenatal and post-natal androgen treatment led to masculinized behavior of female guinea pigs:

Testosterone promoted male typical behavior

Lack of testosterone supported female typical behavior

This led to the organizational-activational hypothesis

Organizational effects: Permanent changes in brain that have long lasting effects

Activational effects: Temporary or transient behaviors or consequences

Natural History in Youth and Adolescents

Many gender dysphoric prepubertal children no longer fulfill criteria for gender dysphoria with onset of puberty. Persisters report greater magnitude of gender dysphoria and have often undergone social transition during childhood. Persisters “believed” that they were affirmed gender.

Gender dysphoria typically persists in youth presenting in adolescence. Distress is often exacerbated with onset of puberty.

Rosenthal SM. JCEM 2014;99:4379
Dutch Outcome Experiences

Puberty Suppression at 12 years (Tanner 2 puberty)

Cross sex hormone treatment at 16 years

Gender affirming surgery at 18 years

22 natal males
33 natal females

Following cross-sex hormone treatment and genital reassignment surgery, gender dysphoria was largely resolved in these patients. Their well-being and functioning in society were fairly comparable to peers. None regretted the treatment.

de Vries et al., Pediatrics 2014;134;696
Limitations of Dutch Outcome Study

Small sample size
No information of physical side effects
No information on bone health
No information on satisfaction with sexual functions
No long term (10-20 year) outcome data

de Vries et al., Pediatrics 2014:134:696
Functional MRI (fMRI)

- Volumes of specific brain regions
- Activation of specific brain regions
- Task-driven activation of specific regions
Comparison Groups:
- Women with CAIS (46,XY)
- Control women (46,XX)
- Control men (46, XY)

- Men showed greater amygdala activation to sexual images than did either typical women or women with CAIS
- Control women and women with CAIS had highly similar patterns of brain activation
- Y chromosome is insufficient for male-typical human brain responses
- Cannot exclude the effect of social experience on the brain responses of women with CAIS as all were raised as girls

Comparison Groups:

- Women with CAIS (46,XY)
- Control women (46,XX)
- Control men (46, XY)

Mental rotation test using fMRI

Control men showed greater activation in inferior parietal lobe than control women

Individuals with CAIS showed female-like pattern.

Conclusion: Sex differences in regional brain function during mental rotation appear to be more related to gonadal hormone exposure rather than genetic sex.

Van Hemmen J, et al. Cerebral Cortex 2016;26:1036-45
Control girls showed increased activation of frontal brain regions compared to control boys for mental rotation task (MRT).

Girls with GD showed decreased right frontal activation compared to control girls prior to T treatment.

After T treatment, girls with GD and boys showed increases in brain areas implicated in mental rotation.

Limitations:
Groups differed because girls with GD were on GnRH agonist
Possible effects of menstrual cycle
Girls with GD share interests and hobbies with boys

Nevertheless, these findings suggest atypical sexual differentiation of the brain in natal girls with GD and provide new evidence for organizational and activational effects of testosterone on visuospatial cognitive functioning.
Distinct brain regions have different response patterns/programs to the sex-specific signals which likely involves cell specific responses, cell-to-cell communication, membrane and nuclear hormone receptors, and local steroid synthesis.

Environmental factors, e.g. endocrine disruptors, stress, differences in maternal behavior, social expectations, & learned behaviors.
Pathways involved in Sexual Differentiation of the Brain

Gene Dosage
Mosaicism
Epigenetics
Astrocytes
Membrane steroid hormone receptors
De novo CNS steroidogenesis
Aromatization
Retinoic acid
PKA
Apoptosis
EDCs
PGE2

Cell death & survival
Local and cell-to-cell communication
Hormones
Glutamate & GABA
Chromosome differences

Arnold and Chen. Frontiers in Neuroendocrinology 2009;30:1
Multiple origins of sex differences in the brain.
Gender variations are not disorders

Gender identity may be fluid and is not binary

Presentations of gender identity are diverse and can vary over time even in the same person

Gender reflects interweaving of biology, development, socialization, culture, and context

Gender is primarily informed by individual’s cognitions and emotions, not genital structures

Ethical Considerations

- Respect for autonomy
- Nonmaleficence ("do no harm")
- Beneficence
- Competency, decision-making, and consequentiality
- Consistent and persistent

Mann et al., Journal of Adolescence 1989;12:265
Team Approach

- Pediatric endocrinologists
- Parents
- Behavioral health/Social Work
- Adolescent physicians & healthcare providers
- PCP(s)
- Parent support groups
- Surgeon(s)

Patient
Mary Cassatt
1844-1926

Thank you

Andy Warhol
1928-1987