Guidelines for the Clinical Care of Persons with Gender Dysphoria

Friday, May 27, 2016
2:15 – 5:00 PM
25th Annual Scientific and Clinical Congress
American Association of Clinical Endocrinologist
Orlando, Fla.

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ACKERMAN INSTITUTE FOR THE FAMILY
NEW YORK, NEW YORK

DISCLOSURES

No Grant or Financial Support
No Board memberships
No Company Ownership

All Medications Discussed
Do Not Have FDA Approval for the Indications Discussed
BEGINNING
IMPORTANT ISSUES

1. Develop Effective Conversations with Transgender Persons
2. Address Important Issues for Transgender Care
3. Initiate Core Discussions
4. Prevent Misunderstandings
5. Address Social and Health Issues of Transgender Persons

GENDER DYSPHORIA: COMPLEXITY

1. Mental Health Professionals
2. Parents/Spouses/Children
3. Friends
4. Work and Professional Associates
5. Health Insurance
6. Name Change
7. ID Change
8. Letter for Medical Recommendations
9. Voice Therapy
10. Facial and Body Surgery
11. Hormone Treatment
12. Genital Surgery
13. Mastectomy
14. Gonadectomy
**WAT IS GENDER DYSPHORIA?**

**NOT GENDER IDENTITY DISORDER**

**NOT TRANSSEXUALISM**

**NOT GENDER NONCONFORMING PEOPLE**

**WHY DOES GENDER DYSPHORIA OCCUR?**

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**GENDER DYSPHORIA: LESS COMPLEX**

Characteristics that Define Persons as “men” and “women” without regard to one’s specific identity;

2. **NATAL SEX:** Sex Determined During Pregnancy and at Birth by Genetic and Developmental Factors;

3. **GENDER IDENTITY:** Inherent Personal Sense of Being Male or Female
4. **GENDER NONCONFORMITY:** The extent to which a person’s gender identity, gender role or gender expression differs from cultural norms of the person’s natal sex;

5. **Transgenderism:** Persons who identify, to varying degrees, with the opposite sex, not the natal sex;

6. **Transsexualism:** Individuals who seek physical transition (hormonal and/or surgical) to the gender opposite that of the natal sex.

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**Gender Dysphoria**

- Gender Dysphoria is a psychological condition, usually appearing in childhood, that causes varying degrees of distress based upon discrepancies between biological characteristics and role expectations AND perceptions of gender. This distress gets worse when the physical manifestations of puberty begin, enhancing social dissonance. When adaptive measures allow assumption of the gender of natal sex into adulthood, associated with hetero- or homosexual roles, persistent Gender Dysphoria may exacerbate distress at any time.

rCBF
Regional Cerebral Blood Flow
Oxygen-15 Water Given During Pet Scan

WHAT IS TRANSGENDER?

The World Professional Association of Transgender Health defines gender dysphoria as the "discomfort or distress that is caused by a discrepancy between a person's gender identity and that person's sex assigned at birth (and the associated gender role and/or primary and secondary sex characteristics)."

The main purpose of treatment is to lessen the dysphoria, so patients may seek different objectives. In the early days of treatment, clinicians often would treat only patients committed to following all the way through with changing their biological sex to make a "whole" male or female. But now the focus is on patient-directed outcomes, which can make the role of endocrinology and hormone treatment that much more important.

WHY DO PEOPLE HAVE GENDER DYSPHORIA?

ASK NEUROSCIENTISTS

Ventral Right Putamen

rCBF
Regional Cerebral Blood Flow
Oxygen-15 Water Given During Pet Scan

Ventral Right Putamen

**Neuroimaging Differences in Spatial Cognition between Men and Male-to-Female Transsexuals Before and During Hormone Therapy**

J Sex Med 2010;7:1858–1867
AUDITORY EVENT SEGMENTATION

DEFAULT MODE

COGNITIVE NEUROSCIENCE NETWORKS

- Genes
- Developments
- Natal
- Pu
- ber
- ty
- Social
- Environment
- Hormones
- Gender
- Sex
- Preferences
1. **SEX**: Biological and Physiological Characteristics that Define Persons as “men” and “women” without regard to one’s specific identity;

2. **NATAL SEX**: Sex Determined During Pregnancy and at Birth by Genetic and Developmental Factors;

3. **GENDER IDENTITY**: Inherent Personal Sense of Being Male or Female
4. **GENDER NONCONFORMITY:** The extent to which a person’s gender identity, gender role or gender expression differs from cultural norms of the person’s natal sex;

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Gender Dysphoria

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"The original copy of any writing
An original is stiled the protocol, **scriptura matrix**: And if the Protocol, which is the root and the foundation of the instrument, does not appear, the instrument is not valid.”
5. Medications

a. Estrogens
   - Spironolactone
   - Cyproterone acetate**
   - Goserelin acetate
   - Finasteride
   - Dutasteride

b. Antiandrogens
   - Progestins
   - Medroxyprogesterone
   - Micronized progesterone

(c) GnRH agonists, (d) Anti-androgens
Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People

The World Professional Association for Transgender Health

7th Version | www.wpath.org

1. This is the seventh version of the Standards of Care. The original SOC were published in 1979. Previous revisions were in 1981, 1985, 1990, 1998, and 2009.
Why Two Phases?

Why not just initiate cross-gender Hormones?

Hormone Therapy for Adolescents

• Goal: Arrest pubertal development of unwanted characteristics of anatomic (natal) sex
Boys (40) with GID
20% GID Persists as adult

Girls (25) with GID
12% GID Persists as adult

For adolescents and adults:
70% persist (Cohen-Kettenis)

Bisexual/homosexual:
Boys – 42.5%  Girls – 32%

Why Two Phases?
Why not just initiate cross-gender Hormones?
Treatment Plan*

PHASE ONE

• Diagnostic evaluation

• Begin pubertal delay with GnRH blocker
  
  Females at Tanner breast stage 2-3
  Males at testicular size 6-8 ml

• Triptorelin Therapy for Adolescents
  3.75 mg IM monthly, after 2 weeks

PHASE TWO

• Age 16 begin cross sex hormones
• Age 18+ consider for surgery

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2.3 Recommendation
We recommend that GnRH analogs be used to achieve suppression of pubertal hormones. (1★★★★)

TABLE 9. Protocol induction of puberty

| Induction of female puberty with 17-β estradiol, increasing the dose every 6 months: |
|---------------------------------|--------------------------------------------------|
| 5 μg/kg/d                        | 10 μg/kg/d                                       |
| 15 μg/kg/d                       | 20 μg/kg/d                                       |
| Adult dose = 2 mg/d              |                                                  |

| Induction of male puberty with testosterone esters, increasing the dose every 6 months: |
|---------------------------------|--------------------------------------------------|
| 25 mg/m² per 2 wk im           | 50 mg/m² per 2 wk im                            |
| 75 mg/m² per 2 wk im           | 100 mg/m² per 2 wk im                           |
Why Two Phases?

Why not just initiate cross-gender Hormones?


Establishment of detailed reference values for luteinizing hormone, follicle stimulating hormone, estradiol, and progesterone during different phases of the menstrual cycle on the Abbott ARCHITECT® analyzer.

Outcomes

Avg E2 = 96 pg/ml

Estradiol

135 pg/ml
Protocol: Transition Female to Male

Phase 1 (Infrequent) Cessation of Menses SOC
- Medroxyprogesterone
- Cyproterone Acetate
- + GnRH Agonist
- Testosterone

Phase 2 – Testosterone (Gradual)
- Transdermal Testosterone
- Weekly IM Testosterone
- Testosterone Undecanoate q 3 months (Europe)
- Testosterone pellets implant

GOAL: Testosterone – 240 – 950 ng/dl
Protocol: Transition Female to Male

1. Testosterone Undecanoate 1000 mg IM q 12 weeks
2. Increase BP: 129/81 to 134/84 p= 0.04
3. All patients reported one additional menses; none thereafter
4. Acne ("troublesome") 14.3%
5. Shaving in 12 months - 77%

The dose of Testosterone required to achieve average male levels, free and total, will vary over time due to changes in metabolism, SHBG binding and aromatase activity. In addition, transdermal absorption changes with time. The Dose should be adjusted based on serum levels.

Why Two Phases?

Why not just initiate cross-gender Hormones?
Testosterone Suppression by Estradiol

Testosterone Dose Response Curve

ADULT PROTOCOL

MATURE MEN

Testosterone

Dose Response Curve

TRANS WOMEN

Outcomes
Protocol: Transition Male to Female
Phase 1 (OR Simultaneously)
Two–Three (12) Months Androgen Suppression
1. Cyproterone Acetate – 50 mg/day
2. Spironolactone 100 – 200 mg/day
3. GnRH Analog
4. Medroxyprogesterone + GnRH Agonist
   Gradual Increase MP – 10-40 mg/day
   GnRH Agonist Monthly x2
5. Finasteride - ? Anti-Androgen; Hair Loss

GOAL: Testosterone < 50 ng/dl
Protocol: Transition Male to Female

Phase 1
Long Term Suppression
- Progestin/Anti-androgen
- GnRHa (Europe)
- Histrelin Implant (Adolescent)

Phase 2
Gradual Addition of Estradiol
- Oral, IM, Patches

**GOAL:** Estradiol 100 – 200 pg/ml
Maintain Testosterone Suppression
Protocol: Transition Male to Female

1998 - 2013

Two – Three Months
Medroxyprogesterone
Gradual Increase MP – 10-40 mg/day
GnRHa x 2 months

Gradual Addition of Estradiol
Oral, IM, Patches

Check LH and Testo 6-8 weeks
After GnRHa agonist

![Graph showing changes in hormone levels over time]
**Male-to-Female**

**Estrogen therapy options**
- Estradiol 2.0-6.0 mg PO daily
- Estradiol patch 0.1-0.4 mg TD twice weekly
- Estradiol valerate 5-30 mg IM every 2 weeks

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**Phase/Step One**

<table>
<thead>
<tr>
<th>Progestins</th>
<th>GnRH Analogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progesterone 20-60 mg PO daily</td>
<td>Medroxyprogesterone acetate 150 mg IM every 3 months</td>
</tr>
<tr>
<td>Cyproterone acetate 50-100 mg PO daily</td>
<td>GnRH agonist (leuprolide) 3.75-7.5 mg IM monthly</td>
</tr>
<tr>
<td>GnRH agonist (leuprolide) 100-200 mg PO daily</td>
<td>Histrelin Implant 50mg implanted every 12 months</td>
</tr>
<tr>
<td>Spironolactone 100-200 mg PO daily</td>
<td>Finasteride 1 mg PO daily</td>
</tr>
</tbody>
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**Phase/Step Two**

**Controversies**

1. Certainty of Diagnosis
2. Role of Mental Health Professional
3. Age of Pubertal Suppression
4. Protocol Strategies
   a. Endogenous Hormones
   b. Hormone Dose
   c. Use of Progestins
   d. Complications – MTF FTM
5. Surgery – Age & Hormones
6. Transsexual vs. Transgender
QUESTIONS