Care of the Transgender Adolescent

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Disclosures

- None
Educational Goals

- To describe the current understanding of gender and gender dysphoria
- To describe current management for transgender individuals:
  - Psychosocial
  - Medical
  - Surgical
Terminology

- **Gender Role**
  - Public expression of gender role

- **Gender Identity**
  - Fundamental sense of one being male, female or indeterminate sex; core gender identity

- **Sexual orientation**
  - The sex the person is physically attracted to

- **Gender Dysphoria (GD)**
  - DSM-V-diagnosis
  - Strong persistent cross-gender identification, combined with a persistent discomfort with one’s sex or sense of inappropriateness in the gender role of that sex causes clinically significant distress

- **Gender non-conformity**
  - Gender identity, role, or expression differs from the cultural norms

- Trans, MtF, FtM, affirmed female, affirmed male, cis-gender genderqueer, trans-woman, trans-man, gender fluid, agender.
Historical Perspectives

- Magnus Hirschfeld (1868-1935)
- Harry Benjamin (1885 – 1986)

- Coined the term “transsexual” in 1923
- 1966 *The Transsexual Phenomenon*
- 1979 the Harry Benjamin International Gender Dysphoria Society (later WPATH)

- Pioneered medical responses in an attempt to have individuals live a gender appropriate lifestyle.
Historical Background

- Christine Jorgensen had the first official “sex change operation” in 1952 in Denmark.

- Michael Dillon was first female to male to undergo phalloplasty in 1946.
ETIOLOGY?

Aydian Dowling, runner up for Men’s Health 2015 “Ultimate Guy” competition
Etiology

- Role of hormonal imprinting on gender identity formation?

- Natural experiment: androgenization and male identity:
  - Congenital adrenal hyperplasia
  - Complete androgen insensitivity
Etiology

- Genetic mechanisms
  - Twin studies \((Behavior\ Genetics,\ 2002;\ 32\ (4):\ 251–257.)\)
  - Vanishing twin

- Maternal immunization against the H-Y antigen and birth order
  - Immunization of some mothers to Y-linked antigens by each succeeding male fetus

- Neuroanatomic and neurofunctional studies
  - Postmortem
  - Live brain-imaging studies \((Nature,\ 1995;\ 378\ (6552):\ 68–70.)\)
Phenomenon in Children

- Children as young as age two may show features that could indicate GD

- Heterogeneity
  - Some children demonstrate extremely gender-nonconforming behavior and wishes, accompanied by persistent and severe discomfort with their primary sex characteristics
  - In other children, these characteristics are less intense or only partially present

- Common to have co-existing psychiatric condition
  - Anxiety
  - Depression
  - Autism

- In most children, gender dysphoria will disappear before, or early in, puberty (80%)
Phenomenon in Adolescents

- Persistence
  - More extreme gender nonconformity in childhood
  - Worsened with development of secondary sexual characteristics in adolescence

- Or new onset: many adolescents and adults presenting with GD do not report a history of childhood gender-nonconforming behaviors

- Delaying proper diagnosis can lead to significant psychological consequences
  - Suicide attempts (41% vs 1.6%) (Injustice Every Turn: A Report of the National Transgender Discrimination Survey, 2011).
Brazilian model Valentina Sampaio graces the cover of French Vogue in March of 2017.
Epidemiology

- Recent years have seen marked increase of referrals in Europe and North America
  - 1:2000 (or about 0.05%) in the Netherlands and Belgium (Olyslager, Femke; Conway, Lynn, 2008)
  - 0.5% of Massachusetts adults (Am J Public Health, 2012; 102 (1): 118–222)
  - 1.2% of New Zealand high-school students (Journal of Adolescent Health; 2014; 55 (1): 93–9)
Epidemiology

- **Difference in natal sex transitioning**  
  - Adults
    - 3x more likely to be male to female
  - Childhood
    - the sex ratio is close to 1:1.

- **WPATH (data from 2003/2004):**
  - Under age 12 - the male/female ratio 6:1 to 3:1
  - Older than age 12 - ratio 1:1
Transgender youth: prevalence

- Minnesota Student Survey, grades 9 and 11
  - Total 81,885 participants, 80,929 with gender responses
  - “Do you consider yourself transgender, gender fluid, or unsure about your gender identity?”
  - Assessments of race, economic hardship, adolescent risk factors, & adolescent protective factors
  - 2,168 (2.7%) positive identification as transgender or gender nonconforming
    - Twice as high among birth assigned females (3.6%) as birth assigned males (1.7%)

Creating an inclusive clinical environment

- **National LGBT Health Education Center**
  - [https://www.lgbthealtheducation.org/](https://www.lgbthealtheducation.org/)
  - Offers training materials for front desk staff, supportive health care staff, and providers

- “How would you like to be addressed?” at check in

- **Gender-inclusive intake forms**
  - Collecting data on gender identity and sexual orientation has been recommended by the Joint Commission

- **Family or non-gendered bathrooms**

The Joint Commission. Advancing effective communication, cultural competence, and patient- and family-centered care for the lesbian, gay, bisexual, and transgender (LGBT) community: a field guide. Oak Brook, IL; Joint Commission; 2011. Available at www.jointcommission.org/assets/1/18/LGBTFieldGuide.pdf
Creating an inclusive clinical environment

What is your current gender identity? (Check one):

- Male
- Female
- Transgender Male/Trans Man/Female-to-Male (FTM)
- Transgender Female/Trans Woman/Male-to-Female (MTF)
- Genderqueer, neither exclusively male nor female
- Additional Gender Category/(or Other), please specify: ______________
- Choose not to disclose

What sex were you assigned at birth on your original birth certificate? (Check one):

- Male
- Female
- Choose not to disclose
Diagnosis

"Little Boy in a Red Dress" William Matthew Prior
(1806-1873)
ICD-10 criteria for transsexualism and gender identity disorder of childhood

- The desire to live and be accepted as a member of the opposite sex
  - usually accompanied by the wish to make his or her body as congruent as possible
  - Not related to a social benefit

- The transsexual identity has been present persistently for at least 2 years

- The disorder is not a symptom of another mental disorder or a genetic, intersex, or chromosomal abnormality
# DSM-V Gender Dysphoria

## Table 3. Diagnosis of transsexualism or gender dysphoria

**TRANSSEXUALISM (F64.0)**

**ICD 10**

Desire to live and be accepted as a member of the opposite sex, usually accompanied by the wish to make his or her body as congruent as possible with the preferred sex through surgery and hormone treatment

Transsexual identity has been present persistently for at least 2 years

Is not a symptom of another mental disorder or a chromosomal abnormality

**GENDER DYSPHORIA IN ADULT**

**DSM-5**

A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months duration, as manifested by at least **TWO** of the following:

a. Marked incongruence between one's experienced/expressed gender primary and/or secondary sex characteristics

b. A strong desire to be rid of one's primary and/or secondary sex characteristics because of marked incongruence with one's experienced/expressed gender

c. A strong desire for the primary and/or secondary sex characteristics of the other gender

d. A strong desire to be of the other gender (or some alternative gender different from one's assigned gender)

e. A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender)

f. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender)

The condition is associated with clinically significant distress or impairment in social, occupational or other important areas of functioning.

Specify if: **With a disorder of sex development** (e.g. congenital adrenogenital disorder such as congenital adrenal hyperplasia or androgen insensitivity syndrome)

Specify if: **Posttransition**: The individual has transitioned to full-time living the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one cross-sex medical procedure or treatment regimen—namely, regular cross-sex hormone treatment or gender reassignment surgery confirming the desired gender.

**Sources:**

- ICD-10: *International Classification of Diseases 10th revision*
- DSM-5: *Diagnostic and Statistical Manual of Mental Disorder Fifth Edition*
Diagnostic assessment and psychotherapy

- Clinician making the diagnosis must be able to
  - Make a distinction between GD and conditions that have similar features
  - Diagnose accurately psychiatric conditions
  - Undertake appropriate treatment

- WPATH SOC guidelines recommend that diagnosis be made by a mental health professional (MHP)

- In the case of children or adolescents the MHP must also be trained in child and adolescent developmental psychopathology.
Management

Avery Jackson, age 9
National Geographic Special Issue: Gender Revolution, January 2017
Management of GD

- Multidisciplinary effort with a focus on hormone therapy:
  - Diagnostic assessment
  - Psychotherapy or counseling
  - Real-life experience
  - Hormone Therapy
  - Surgical therapy
Endocrine Treatment of Transsexual Persons

- **WPATH - Standards of Care**

- **Endocrine Treatment of Transsexual Persons: An Endocrine Society Clinical Practice Guideline**
  - *J Clin Endocrin Metab, June 9, 2009*
  - Sponsored by European Society of Endocrinology (ESE), European Society of Pediatric Endocrinology (ESPE), Lawson Wilkins Pediatric Endocrine Society (LWPES), and World Professional Association for Transgender Health (WPATH)
Mental health care

- Transgender youth are significantly more likely to report bullying, suicidal thoughts, suicidal ideation in the past year.
- Requirement of 2009 Endocrine Society Guidelines for the Treatment of Transsexual Persons
- “Gate-Keeping?”
- “Persisters” vs “Desisters”

Social Support

- Patients who experience family support when they come out have lower suicide attempt rates

  - Injustice at Every Turn: A Report of the National Transgender Discrimination Survey, 2011
Transgender youth: prevalence

<table>
<thead>
<tr>
<th>Risk behaviors</th>
<th>Transgender and gender nonconforming (n = 2,168)</th>
<th>Cisgender (n = 787)</th>
<th>p value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance use (past 30 days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoked cigarettes</td>
<td>297 (15.2)</td>
<td>4,315 (5.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Drank alcohol</td>
<td>458 (23.4)</td>
<td>12,539 (17.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Binge drinking</td>
<td>219 (11.2)</td>
<td>6,099 (8.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Smoked marijuana</td>
<td>337 (17.4)</td>
<td>7,758 (10.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sexual behaviors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever had sex</td>
<td>572 (30.0)</td>
<td>15,749 (22.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>≥ 2 partners (past year)</td>
<td>296 (15.5)</td>
<td>6,076 (8.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No condom at last sex</td>
<td>289 (15.3)</td>
<td>5,926 (8.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No birth control at last sex</td>
<td>224 (40.7)</td>
<td>3,702 (25.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intoxicated at last sex</td>
<td>124 (21.8)</td>
<td>2,257 (14.4)</td>
<td>&lt;.001</td>
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<tr>
<td>Emotional distress</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressive symptoms (PHQ-2 ≥3)</td>
<td>1,155 (57.9)</td>
<td>15,848 (21.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Self-harm (past year)</td>
<td>1,076 (54.8)</td>
<td>10,650 (14.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Suicidal ideation (ever)</td>
<td>1,302 (61.3)</td>
<td>14,812 (20.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Suicide attempt (ever)</td>
<td>609 (31.0)</td>
<td>5,286 (7.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Bullying victimization (past 30 days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical</td>
<td>526 (25.1)</td>
<td>9,841 (12.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Relational</td>
<td>1,091 (52.2)</td>
<td>24,764 (32.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cyber</td>
<td>582 (27.6)</td>
<td>9,519 (12.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Prejudice-based reason: gender</td>
<td>737 (35.3)</td>
<td>3,658 (4.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Prejudice-based reason: gender expression</td>
<td>979 (46.9)</td>
<td>11,658 (15.0)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Protective factors</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>p b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal assets (range: 1-4)</td>
<td>2.56 (.61)</td>
<td>2.97 (.59)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Family connectedness (range: 1-5)</td>
<td>3.53 (.96)</td>
<td>4.27 (.76)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Student-teacher relationships (range: 1-4)</td>
<td>2.80 (.64)</td>
<td>3.07 (.58)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Feel safe in community (range: 1-4)</td>
<td>3.19 (.66)</td>
<td>3.55 (.53)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Individualized Management

- Not every individual with GD feel the need to masculinize or feminize their body!
Treatment Options

- Psychotherapy
  - Exploring gender expression and role
    - May involve living part time or full time in the gender role consistent with one’s gender identity
    - Promoting resilience
The Real Life Experience

● The act of fully adopting a new or evolving gender role or gender presentation in everyday life

● Essential to the transition to a gender role that is congruent with the patient’s gender identity

● Assists both the patient and the MHP in their judgments in how to proceed

● Living 12 months full-time in the desired gender role is recommended.
Social Transition in Childhood

- Social transitions in early childhood do occur within some families with early success.

- This is a controversial issue, and divergent views are held by health professionals.
Medical Treatment Options: Physical Interventions
Treatment Options

- **Physical Interventions**
  - **Fully reversible**
    - GnRH agonists to suppress estrogen and/or testosterone
    - Medroxyprogesterone/spironolactone
  - **Partially reversible**
    - Hormonal intervention to feminize or masculinize the body
  - **Irreversible**
    - Surgical procedures
Eligibility and Readiness Criteria

- Adolescents are eligible and ready for GnRH treatment if they:
  - Fulfill DSM V or ICD-10 criteria
  - Experienced puberty to at least Tanner stage 2
  - Pubertal changes that have resulted in an increase of their GD
  - Do not suffer from psychiatric co-morbidity that interferes with the diagnostic work-up or treatment
  - Adequate psychological and social support during treatment
  - Demonstrate knowledge and understanding of the expected outcomes of treatment
  - Demonstrate knowledge of social risks and benefits of sex reassignment
Eligibility and Readiness Criteria

- Adolescents are eligible for cross-sex hormone treatment if they:
  - Fulfill the criteria for GnRH treatment, AND
  - Are 16 years or older

- Eligibility criteria has not been evaluated in formal studies
  - Few small follow-up/questionnaire studies
    - Good post-op results
    - Psychotherapy before medical evaluation
Physical Interventions
Physical Interventions WPATH-SOC

- Before any physical intervention is considered, extensive exploration of psychological, family and social issues should be undertaken.

- One letter from a mental health professional is required for instituting hormone therapy or breast surgery.

- Two letters are required for genital surgery (or one letter signed by two mental health professionals).

- Irreversible physical interventions should be delayed as long as is clinically appropriate.
  - Fluidity may return at a later stage.
Fully Reversible
Fully Reversible

- GnRH analogues
- Medroxyprogesterone
- Anti-estrogens
- Anti-androgens
Physical Benefits

- Preventing the need for mammoplasties
- Preventing menarche/menses
- Allowing for longer period of growth in biological females via delayed epiphyseal closure
- Preventing skeletal changes, especially facial bones, that accentuate brow, zygoma, mandible, and to prevent development of an Adam’s apple
- Preventing unwanted phallic growth and psychologically spontaneous erections
- Preventing permanent male voice and virilized facial and scalp hair patterns
Negative Effects

- Expensive!!

- Possible impact on brain development
  - Brain undergoes major reorganization during the adolescent period

- Arrest of the normal pubertal bone mass increase
  - May catch-up once cross-sex hormone treatment is begun

- Insufficient penile tissue for penile inversion vaginoplasty techniques.
Partially Reversible Interventions

Cross-Sex Steroids
Cross Sex Steroids

- Pubertal development of the desired, opposite sex be initiated at the age of 16 years (earlier in selected cases), using gradually increasing dose schedule of cross-sex steroids

- Following repeat intensive psychometric evaluation
Cross Sex steroids

- There are no published reports of randomized clinical trials comparing safety and efficacy
- A wide variety of regimens have been published
  - Cross sex hormone after puberty suppression
  - Cross sex hormone without prior use of puberty suppression
FtM

- Relatively straightforward regimens

- Testosterone usually sub-cutaneous or intra-muscular
  - Try to keep testosterone in normal male range (320-1000 ng/dL)
  - Teach patient to self-administer
Masculinizing effects in female-to-male transsexual persons

<table>
<thead>
<tr>
<th>Effect</th>
<th>Onset</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin oiliness/acne</td>
<td>1-6 months</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Facial/body hair growth</td>
<td>6-12 months</td>
<td>4-5 years</td>
</tr>
<tr>
<td>Scalp hair loss</td>
<td>6-12 months</td>
<td>****</td>
</tr>
<tr>
<td>Increased muscle mass/strength</td>
<td>6-12 months</td>
<td>2-5 years</td>
</tr>
<tr>
<td>Fat redistribution</td>
<td>1-6 months</td>
<td>2-5 years</td>
</tr>
<tr>
<td>Cessation of menses</td>
<td>2-6 months</td>
<td>******</td>
</tr>
<tr>
<td>Clitoral enlargement</td>
<td>3-6 months</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Vaginal atrophy</td>
<td>3-6 months</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Deepening of voice</td>
<td>6-12 months</td>
<td>1-2 years</td>
</tr>
</tbody>
</table>

**** Prevention and treatment as recommended for biological men.

***** Menorrhagia requires diagnosis and treatment by a gynecologist.
MtF

- **Male-to-Female**
  - More complex than FTM regimen

- **Estrogen**
  - Oral, transdermal (benefit less VTE), or parenteral
  - Serum estradiol levels should be maintained <200 pg/dL (premenopausal women)
  - Testosterone <55ng/dl
  - Conjugated estrogens or synthetic estrogens can not be monitored by blood tests

- **Antiandrogens**
  - Spironolactone
## Feminizing effects in male-to-female transsexual persons

<table>
<thead>
<tr>
<th>Effect</th>
<th>Onset</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Redistribution Body Fat</td>
<td>3-6 months</td>
<td>2-3 years</td>
</tr>
<tr>
<td>Decrease Muscle Mass and Strength</td>
<td>3-6 months</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Softening of Skin/Decreased Oiliness</td>
<td>3-6 months</td>
<td>Unknown</td>
</tr>
<tr>
<td>Decreased libido</td>
<td>1-3 months</td>
<td>3-6 months</td>
</tr>
<tr>
<td>Decreased Spontaneous Erections</td>
<td>1-3 months</td>
<td>3-6 months</td>
</tr>
<tr>
<td>Male Sexual Dysfunction</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Breast Growth</td>
<td>3-6 months</td>
<td>2-3 Years</td>
</tr>
<tr>
<td>Decreased Testicular Volume</td>
<td>3-6 months</td>
<td>2-3 Years</td>
</tr>
<tr>
<td>Decreased Sperm Production</td>
<td>Unknown</td>
<td>&gt; 3 years</td>
</tr>
<tr>
<td>Decreased Terminal Hair Growth</td>
<td>6-12 months</td>
<td>&gt; 3 years*</td>
</tr>
<tr>
<td>Scalp Hair</td>
<td>No Regrowth</td>
<td>**</td>
</tr>
<tr>
<td>Voice Changes</td>
<td>None</td>
<td>***</td>
</tr>
</tbody>
</table>

* Complete removal of male sexual hair requires electrolysis and/or laser
** Familial scalp hair loss may occur if estrogens are stopped.
*** Treatment by speech pathologists for voice training is most effective.
Risks of Cross-Sex Hormones
Risks Associated with Hormone Therapy

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Feminizing Hormones</th>
<th>Masculinizing hormones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likely increased risk</td>
<td>• Venous thromboembolic disease</td>
<td>Polycythemia</td>
</tr>
<tr>
<td></td>
<td>• Gallstones</td>
<td>• Weight gain</td>
</tr>
<tr>
<td></td>
<td>• Elevated liver enzymes</td>
<td>• Acne</td>
</tr>
<tr>
<td></td>
<td>• Weight gain</td>
<td>• Androgenic alopecia (balding)</td>
</tr>
<tr>
<td></td>
<td>• Hypertriglyceridemia</td>
<td>• Sleep apnea</td>
</tr>
<tr>
<td>Likely increased risk with presence of</td>
<td>Cardiovascular disease</td>
<td></td>
</tr>
<tr>
<td>additional risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Possible increased risk</td>
<td>Hypertension</td>
<td>Elevated liver enzymes</td>
</tr>
<tr>
<td></td>
<td>• Hyperprolactinemia or prolactinoma</td>
<td>• Hyperlipidemia</td>
</tr>
<tr>
<td>Possible increased risk with presence of</td>
<td>Type 2 diabetes</td>
<td></td>
</tr>
<tr>
<td>additional risk factors</td>
<td></td>
<td>Destabilization of certain psychiatric disorders</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cardiovascular disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hypertension</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Type 2 diabetes</td>
</tr>
<tr>
<td>No increased risk or inconclusive</td>
<td>• Breast cancer</td>
<td>Loss of bone density</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Breast cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cervical cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ovarian cancer</td>
</tr>
</tbody>
</table>
Follow up during hormone therapy:

**Male-to-Female**
Evaluate patients every 2-3 months in the first year and then 1-2 times per year thereafter to monitor for appropriate signs of feminization and for development of adverse reactions

Measure serum testosterone and estradiol levels every 3 months
  - Serum testosterone levels should be <55 ng/dL
  - Serum estradiol levels should be 100–200 pg/dL
  - Adjust estradiol dosage according to serum levels

Measure serum electrolytes every 2-3 months for the first year if patients are taking spironolactone

Measure serum prolactin levels at baseline, at 12 months following initiation of treatment, and biennially thereafter

**Female-to-Male**
Evaluate patients every 2-3 months in the first year and then 1-2 times per year thereafter to monitor for appropriate signs of feminization and for development of adverse reactions

Measure serum testosterone every 2-3 months until levels are in the normal physiologic range (320–1000 ng/dL)\(^a\)
  - Testosterone enanthate/cypionate: measure between injections
  - Testosterone undecanoate: measure prior to the next injection
  - Transdermal testosterone: measure any time after week 1

Measure estradiol levels during the first 6 months of testosterone treatment or until there is cessation of menses for 6 months
  - Estradiol levels should be <50 ng/dL

Measure complete blood count and liver function tests at baseline and every 3 months for the first year and then 1-2 times per year thereafter
Effects of Cross-Sex Hormones on Adolescents With Gender Dysphoria

<table>
<thead>
<tr>
<th></th>
<th>FTM</th>
<th>MTF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>72</td>
<td>44</td>
</tr>
<tr>
<td><strong>Age (Mean)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Min)</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>(Max)</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Depression</td>
<td>22</td>
<td>13</td>
</tr>
<tr>
<td>▪ Anxiety</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>▪ ADHD</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>▪ HIV</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td><strong>Other Medications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ GnRH agonists/ Puberty Blockers</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>▪ Spironolactone</td>
<td>0</td>
<td>36</td>
</tr>
<tr>
<td>▪ Psychotropic medications</td>
<td>26</td>
<td>13</td>
</tr>
<tr>
<td>▪ HAART</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>
## Outcomes: FTM

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1-3 Months</th>
<th>4-6 Months</th>
<th>Beyond 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>26.0</td>
<td>26.2 (&lt;.0001)</td>
<td>27.2 (&lt;.0001)</td>
<td>27.0 (.0003)</td>
</tr>
<tr>
<td><strong>SBP (mm/Hg)</strong></td>
<td>118</td>
<td>122*</td>
<td>119*</td>
<td>118*</td>
</tr>
<tr>
<td><strong>DBP (mm/Hg)</strong></td>
<td>71</td>
<td>72*</td>
<td>67 (.01)</td>
<td>69*</td>
</tr>
<tr>
<td><strong>HCT (%)</strong></td>
<td>39.4</td>
<td>42.4 (&lt;.0001)</td>
<td>43.0 (&lt;.0001)</td>
<td>44.5 (&lt;.0001)</td>
</tr>
<tr>
<td><strong>HGB (g/dL)</strong></td>
<td>13.5</td>
<td>14.2*</td>
<td>14.3 (.0156)</td>
<td>15.0 (&lt;.0001)</td>
</tr>
<tr>
<td><strong>Total T (ng/dL)</strong></td>
<td>29.5</td>
<td>342.8 (&lt;.0001)</td>
<td>462.6 (&lt;.0001)</td>
<td>424.8 (&lt;.0001)</td>
</tr>
<tr>
<td><strong>Estradiol (pg/dL)</strong></td>
<td>55.1</td>
<td>51.1*</td>
<td>42.9*</td>
<td>46.0*</td>
</tr>
<tr>
<td><strong>Tchol (mg/dL)</strong></td>
<td>151.2</td>
<td>157.4*</td>
<td>160.7*</td>
<td>153.5*</td>
</tr>
<tr>
<td><strong>LDL (mg/dL)</strong></td>
<td>84.5</td>
<td>93.0*</td>
<td>98.3*</td>
<td>90.6*</td>
</tr>
<tr>
<td><strong>HDL (mg/dL)</strong></td>
<td>50.2</td>
<td>44.3 (.0159)</td>
<td>42.9 (0.0030)</td>
<td>45.1 (0.0156)</td>
</tr>
<tr>
<td><strong>TG (mg/dL)</strong></td>
<td>93.2</td>
<td>102.6*</td>
<td>108.5*</td>
<td>98.1*</td>
</tr>
<tr>
<td><strong>TG:HDL Ratio</strong></td>
<td>2.0</td>
<td>2.5*</td>
<td>2.9 *</td>
<td>2.3*</td>
</tr>
<tr>
<td><strong>BUN (mg/dL)</strong></td>
<td>10.7</td>
<td>10.5*</td>
<td>8.3*</td>
<td>6.5*</td>
</tr>
<tr>
<td><strong>Cr (mg/dL)</strong></td>
<td>0.7</td>
<td>0.9*</td>
<td>0.9*</td>
<td>0.8*</td>
</tr>
<tr>
<td><strong>Prolactin (ng/mL)</strong></td>
<td>16.5</td>
<td>26.6*</td>
<td>12.0*</td>
<td>28.1*</td>
</tr>
<tr>
<td><strong>AST (U/L)</strong></td>
<td>18.8</td>
<td>20.1*</td>
<td>25.9*</td>
<td>19.5*</td>
</tr>
<tr>
<td><strong>ALT (U/L)</strong></td>
<td>21.1</td>
<td>21.7*</td>
<td>26.9*</td>
<td>20.0*</td>
</tr>
<tr>
<td><strong>HgbA1c (%)</strong></td>
<td>5.3</td>
<td>5.5*</td>
<td>4.9*</td>
<td>5.3*</td>
</tr>
</tbody>
</table>
### Outcomes: MTF

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1-3 Months</th>
<th>4-6 Months</th>
<th>Beyond 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>23.7</td>
<td>23.0*</td>
<td>23.6*</td>
<td>23.6*</td>
</tr>
<tr>
<td><strong>SBP (mm/Hg)</strong></td>
<td>125</td>
<td>124*</td>
<td>121*</td>
<td>121*</td>
</tr>
<tr>
<td><strong>DBP (mm/Hg)</strong></td>
<td>72</td>
<td>74*</td>
<td>72*</td>
<td>72*</td>
</tr>
<tr>
<td><strong>HCT (%)</strong></td>
<td>43.8</td>
<td>38.3*</td>
<td>40.3*</td>
<td>42.3*</td>
</tr>
<tr>
<td><strong>HGB (g/dL)</strong></td>
<td>14.5</td>
<td>12.7*</td>
<td>13.6*</td>
<td>14.4*</td>
</tr>
<tr>
<td><strong>Total T (ng/dL)</strong></td>
<td>391.7</td>
<td>256.3 (.0128)</td>
<td>233.6 (.0008)</td>
<td>199.3 (.0002)</td>
</tr>
<tr>
<td><strong>Estradiol (pg/dL)</strong></td>
<td>21.6</td>
<td>40.9*</td>
<td>49.9 *</td>
<td>96.4 (&lt;.0001)</td>
</tr>
<tr>
<td><strong>Tchol (mg/dL)</strong></td>
<td>147.8</td>
<td>158.0*</td>
<td>138.2*</td>
<td>142.8*</td>
</tr>
<tr>
<td><strong>LDL (mg/dL)</strong></td>
<td>82.6</td>
<td>95.9*</td>
<td>73.0*</td>
<td>77.4*</td>
</tr>
<tr>
<td><strong>HDL (mg/dL)</strong></td>
<td>48.2</td>
<td>47.4*</td>
<td>51.2 *</td>
<td>49.3*</td>
</tr>
<tr>
<td><strong>TG (mg/dL)</strong></td>
<td>93.5</td>
<td>77.9*</td>
<td>74.7*</td>
<td>83.6*</td>
</tr>
<tr>
<td><strong>TG:HDL Ratio</strong></td>
<td>2.1</td>
<td>1.7*</td>
<td>1.0*</td>
<td>1.9*</td>
</tr>
<tr>
<td><strong>BUN (mg/dL)</strong></td>
<td>14.6</td>
<td>14.9*</td>
<td>15.0*</td>
<td>11.5*</td>
</tr>
<tr>
<td><strong>Cr (mg/dL)</strong></td>
<td>0.7</td>
<td>0.6*</td>
<td>0.7*</td>
<td>0.7*</td>
</tr>
<tr>
<td><strong>Prolactin (ng/mL)</strong></td>
<td>11.9</td>
<td>10.9*</td>
<td>17.5*</td>
<td>20.7*</td>
</tr>
<tr>
<td><strong>AST (U/L)</strong></td>
<td>20.1</td>
<td>24.9*</td>
<td>19.6*</td>
<td>17.5*</td>
</tr>
<tr>
<td><strong>ALT (U/L)</strong></td>
<td>25.4</td>
<td>23.5*</td>
<td>15.2 (.0141)</td>
<td>17.3 (.0217)</td>
</tr>
</tbody>
</table>
“We recommend that all transsexual individuals be informed and counseled regarding options for fertility prior to initiation of puberty suppression in adolescents and prior to treatment with sex hormones of the desired sex in both adolescents and adults”

- Endocrine Society Clinical Practice Guidelines for the Treatment of Transsexual Persons
Partially Reversible Methods Effect on Fertility

- **Estrogen:**
  - Prolonged exposure of the testes to estrogen has been associated with testicular damage
  - May decrease libido.
  - Reduces nocturnal erections, with variable impact on sexually stimulated erections.

- **Testosterone:**
  - Reduces fertility, although the degree and reversibility are unknown.
  - Can induce permanent anatomic changes in the developing embryo or fetus.

Pregnancy has been reported in FTM individuals on testosterone
Fertility Options: Male-to-Female

- **Sperm Banking (Sperm Cryopreservation)**
  - Sperm have been successfully after Tanner 3 has been reached
  - In boys around 12 who are peri-pubertal may be a candidate for testicular sperm extraction
    - Has to be done in the operating room as it is painful

- **Special Consideration with children and adolescents**
  - May require cessation of hormone therapy prior to sperm retrieval
  - Children on hormone blockers may not have mature sperm to preserve.
Fertility Options: Female-to-Male

- Egg Freezing (Oocyte cryopreservation)
  - Optimally performed prior to testosterone treatment
  - Primarily done after ovarian stimulation
  - ? Response if Tanner 2 and received GnRH
  - Requires transvaginal aspiration of eggs

Case Report:
- Fertility preservation in the transgender patient
  - Posted online on September 25, 2014.
Fertility Options: Adulthood

- **Testicular or Ovarian Tissue Freezing:**
  - It can be an option at age 18 or older, if the teen is thinking about gender confirming surgery.
    - But by then gonads often have been exposed to estrogen and testosterone.
  - Puberty blockers would stop development of the testes and ovaries, so they may require in-vitro maturation of gametes which is still experimental.
Risk of Pregnancy

- Though fertility is compromised:
  - Puberty suppression can be associated with sperm production and ovulation
  - Trans men can become pregnant while on T
  - Trans females may still produce sperm and impregnate female partners.
Pregnancy in Trans Men

- 48% of 25 trans men who answered a web-based questionnaire who were on testosterone prior to pregnancy used no contraceptive.
- 40% used condoms
- 12% abstinence

- 6/25 patients reported pregnancy was not planned
Irreversible Intervention

Sex Reassignment Surgery
Surgical Procedures for Affirmed Males

- Breast/chest surgery
  - Considered before age 18

- Nongenital, nonbreast surgical interventions
  - Voice surgery
  - Liposuction, lipofilling, pectoral implants, and various aesthetic procedures
Surgical procedures for FTM

- Hysterectomy/Salpingo-oophorectomy
  - Unlikely to be screened
  - Possible risk of aromatization of testosterone and endometrial hyperplasia
  - Required in some states to legally change sex

- ? Risk of taking out the ovaries
Surgical Procedures FtM

- Genital surgery
  - Rarely seek genital because final surgical product lacks functionality and has limited cosmetic result
  - High complication risks
  - Reconstruction of the fixed part of the urethra combined with:
    - Metoidioplasty or with phalloplasty
    - Vaginectomy
Metoidioplasty
Phalloplasty
Surgical Procedures for Affirmed Females

- Breast/chest surgery
  - Augmentation mammoplasty (implants/lipofilling);
Surgical Procedures for Affirmed Females

- Nongenital, nonbreast surgical interventions
  - Facial feminization surgery,
  - liposuction,
  - lipofilling,
  - voice surgery,
  - thyroid cartilage reduction,
  - gluteal augmentation,
  - hair reconstruction,
Surgical procedures for MTF

- **Genital surgery:**
  - Penectomy,
  - Orchiectomy,
  - Vaginoplasty,
  - Clitoroplasty,
  - Vulvoplasty
Children’s National Gender Program

- Gender and Sexuality Development Program 202-476-4172
  - David Call, MD - Psychiatrist
  - Martine Solanges, MD - Psychiatrist
  - John Strang, PhD - Psychologist
    - Expert in Autism spectrum
  - Veronica Gomez-Lobo, MD - Pediatric Gynecology
  - Lauren Damle, MD - Pediatric Gynecology
  - Rinku Mehra, MD - Pediatric Endocrinology