The Changing Rx of Transgender Adolescents: Impact of GnRHa Pubertal Blockade and Implications for Young Adults and Adults

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Disclosures

- I still have no disclosures. Did I miss something?

- I will discuss some off-label use of GnRH analogues, by generic names.

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Learning Objectives

By the end of this session, learners will be able to

1. Describe recommended ways to follow and care for children and adolescents who are questioning their gender.
2. Identify cases when pubertal blockade may be indicated and when to begin treatment
3. Explain how primary care and specialty clinicians work together when caring for gender dysphoric children and adolescents
Types of Sex/Gender: a Counter to “Biologic Sex”

- Genetic sex
- Chromosomal sex
- Gonadal sex
- Phenotypic sex
- Sex of rearing
- Gender identity vs. Gender role
- Gender attribution
- Sexual orientation/sexual identity
FURTHER STUDIES ON THE TREATMENT OF CONGENITAL ADRENAL HYPERPLASIA WITH CORTISONE

IV. Effect of Cortisone and Compound B in Infants with Disturbed Electrolyte Metabolism

By John F. Crigler, Jr., M.D., Samuel H. Silverman, M.D., and Lawson Wilkins, M.D.

Baltimore

In preceding papers 1-7 the effect of cortisone on various phases of the syndrome of congenital adrenal hyperplasia has been reported. This paper will, therefore, be limited to a discussion of the treatment of infants with this disease who have an associated abnormality of the salt-regulating mechanism of the adrenal. Although this disorder has been recognized for a number of years, its diagnosis and treatment is often a difficult problem; and in general, the prognosis has been poor. With the advent of cortisone,
Getting from FTM

- Goals: stop puberty; gain time/height
  - Virilize (4 cm clitoris)-quite effective
  - Suppress menses (norethindrone, tamoxifen)
  - Remove breasts ~ age 16 (size determines approach-flat chest/areola relocation)

- Methods
  - Androgen Rx: Testosterone injections, gels (BTB), oral (never); may spot from Testost
  - GnRH analogues (histrelin implant)
  - Oophorectomy, Hysterectomy (laparoscopic)-remove cervix-> no paps
Getting from MTF

- Suppress serum Testosterone
  - via GnRHa or Estrogen (4-10 mg/d)
  - or both (1-2 mg/d Estrogen)
- Develop breasts (optimal with GnRHa-induced Testost. suppression)
- *Preserve scalp hair/suppress facial
- Spironolactone and/or Finasteride
- *150/wk for years)
- Suppress erections
- *Limit masculine facial bone strux
- *Voice, hgt, skeleton-> “gender attribution”

*Features that can be reduced even at Tanner 3-5, age 15-19*
Observations/Conclusions from Treating 200 Adults

- Challenge of gender attribution-being “read”
- Genotypic skeleton: habitus, height, acral size, facial bone structure, Adam’s apple
- Male pattern hair loss in MTF
- Lengthened vocal cords in MTF
- Small fortune on electrolysis ($150/wk)
- Losses: partner, family, job, friends
- Increased substance use, depression, self-harm: 3 suicides (45% of unsupported 16-25 yr olds will attempt suicide; FTMs more likely to use fatal method—gun or other violence; MTFs more likely to ingest pills and be resuscitated)
- Maimonides’ commentary on healing
Gender Dysphoria in Children

- Zucker et al- 80% of children exhibiting an opposite gender role “desist” by Tanner 2
- Those 80% who “desist” usually become gender-variant (usually gay) as adults but not transgender
- The 20% who “persist” at Tanner 2 are transgender persons, to be treated according to Endocrine Society 2009 & WPATH2011 guidelines
The Amsterdam Experiment

- Treatment of adolescent transsexuals at Tanner 2-3 (males 12-14; females 10-12) using GnRHa analogues to:
  1. Suppress spontaneous pubertal development
  2. Allow for balanced decision regarding sex reassignment
  3. Achieve optimal final height and bone development
  4. Prevent side effects of pubertal delay via cross-gender sex steroids ~ age 16
The HPG axis and Puberty

kisspeptin neurons

GnRH neurons

pituitary

FSH/LH

gonads

testosterone, estradiol

secondary sexual characteristics

PUBERTY

?
GeMS Requirements

- Tanner 2-5
- In counseling with gender therapist > 6 months
- Referral letter from therapist, recommending medical Rx
- Support of both custodial parents
- No severe psychopathology
Limitations for GnRHa Therapy in the U.S.

- Perception that GID is a psychiatric (DSM-IV), not medical, condition
- Lack of mental health personnel skilled in assessing gender dysphoric children
- Unfamiliarity and anxiety in the pediatric endocrine community concerning medical treatment of GID in children and adolescents
- Prohibitively expensive costs and lack of insurance coverage (BUT changing)
Histrelin implant
### Demographics for All Patients since 1998

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Biological Females</th>
<th>Biological Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>158 (100)</td>
<td>79 (50)</td>
<td>79 (50)</td>
</tr>
<tr>
<td>Age of presentation, mean ± SD*</td>
<td>14.7 ± 3.5</td>
<td>15.1 ± 3.5</td>
<td>14.3 ± 4.0</td>
</tr>
<tr>
<td>Tanner stage, mean ± SD and median**</td>
<td>3.75 ± 1.5</td>
<td>4.0 ± 1.4</td>
<td>3.4 ± 1.5</td>
</tr>
</tbody>
</table>

*First 158 Pts
Age of Declaration of Gender Dysphoria

- MTF
- FTM

*First 158 Pts*
## Psychiatric History

<table>
<thead>
<tr>
<th>Description</th>
<th>N</th>
<th>(%)</th>
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</thead>
<tbody>
<tr>
<td>With psychiatric diagnosis before CHB evaluation*</td>
<td>71</td>
<td>(44.9)</td>
</tr>
<tr>
<td>On psychiatric medications</td>
<td>51</td>
<td>(32.3)</td>
</tr>
<tr>
<td>With prior psychiatric hospitalizations</td>
<td>13</td>
<td>(8.2)</td>
</tr>
<tr>
<td>History of self-mutilation</td>
<td>29</td>
<td>(18.4)</td>
</tr>
<tr>
<td>History of suicide attempt</td>
<td>15</td>
<td>(11.4)</td>
</tr>
</tbody>
</table>

* 25 patients presented with more than one psychiatric diagnosis.
# Psychiatric Diagnoses

<table>
<thead>
<tr>
<th>Disorder</th>
<th>N</th>
<th>% of 60 patients with psychiatric diagnoses</th>
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</thead>
<tbody>
<tr>
<td>Depression</td>
<td>32</td>
<td>53.3</td>
</tr>
<tr>
<td>General Anxiety Disorder</td>
<td>16</td>
<td>26.7</td>
</tr>
<tr>
<td>Bipolar Disorder</td>
<td>9</td>
<td>15.0</td>
</tr>
<tr>
<td>Pervasive Developmental Disorders (non-Austism)</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Eating Disorder</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Attention Deficit Hyperactivity Disorder/Attention Deficit Disorder</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>Autism</td>
<td>2</td>
<td>3.3</td>
</tr>
<tr>
<td>Panic Disorder</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>Post-Traumatic Stress Disorder</td>
<td>2</td>
<td>3.3</td>
</tr>
</tbody>
</table>

*First 158 Pts
New Ped. Academic Programs for Transgender Youth

- Toronto- Sick Kids -Mark Palmert*
- L.A. Children’s- Marvin Belzer, J. Olson
- Vancouver- Dan Metzger
- Cincinnati Children’s Hospital
- Hasbro Children’s, Providence- Forcier*
- UCSF Children’s Hosp-s.- Rosenthal*, Vance*
- NYU Medical Ctr.-Laura Erickson- Schroth*
- Maine Medical Ctr.- Olshan*, Dedekian*, Morris*
- Lurie Children’s, Chicago- Finlayson*

In 2007, n=1
In 2014, n = 35
Other New Centers

- St. John, New Brunswick, Canada (Sanderson*)
- Detroit Children’s (K. Moltz*)
- Morristown (NJ) Med. Center (W. Rosenfeld*)
- Wash. U/St. Louis (K. Platz*)
- Iowa
- On Deck: Columbia, KC, U Wisconsin, Dallas-(Lopez* Et Al)
- Portland Or (Edwards-Leeper*)
- Children’s Hospital of Philadelphia
The Future: Looking brighter

- More insurers adding riders to provide coverage, including universities (35 in USA)
- DSM-VI may delete transgenderism as a psychiatric condition; therefore, medical/surgical benefits will be paid
- Every medical student, house officer will be trained in gender issues, even child psychiatrists
- Transgender individuals will no longer face legalized discrimination
- Optimal care will be modeled by national health services everywhere, so transgender Tanner 2 adolescents needn’t go through a “toxic puberty”
Special Circumstance

- The gender-non-conforming adolescent who has Asperger’s Syndrome
  - 10% of our new patient population
  - Has not shown nor expressed gender issues until past ~2 years
  - Extremely obsessive about desire to be the opposite gender
  - Parents confused: Is this just another obsession?
  - Pubertal patients do seem relieved by pubertal suppression
Scrotal Tissue Expansion