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.

WYLIE HEMBREE MD
COLUMBIA UNIVERSITY MEDICAL CENTER
MOUNT SINAI BETH ISRAEL MEDICAL CENTER
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

WHAT IS GENDER DYSPHORIA?

NOT GENDER IDENTITY DISORDER

NOT TRANSSEXUALISM

NOT GENDER NONCONFORMING PEOPLE
DISCOMFORT WITH THE GENDER PRESCRIBED BY THE NATAL SEX AND THE RESULTING BODY DEVELOPMENT, ESPECIALLY AT PUBERTY

WHY DO PEOPLE HAVE GENDER DYSPHORIA?

ASK NEUROSCIENTISTS


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

Men
MFTS pre HT
MFTS with HT

a
b
A critical role for the right fronto-insular cortex in switching between central-executive and default-mode networks.

AUDITORY EVENT SEGMENTATION

COGNITIVE NEUROSCIENCE NETWORKS

DEFAULT MODE

Daniel Levitin

Gender

Social

Hormones

Environ

Sex

Prefer

Gender

Pu

ber

ty

Natal

Dev
COGNITIVE NEUROSCIENCE NETWORKS

Genes

Dev

Natal

Pu

ber

ty

Social

Environ

Hormones

Gender

Sex

Prefer

PROTOCOL
(Dutch, French, Greek)

A Dictionary of the English Language
A History of the Language
and an
English Grammar
By Samuel Johnson A.M.

“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.”
ENDOCRINOLOGIC TREATMENT OF GENDER IDENTITY DISORDERS

Endocrine Treatment of Male-to-Female Transsexuals Using Gonadotropin-Releasing Hormone Agonist
Erlangen, Germany

Care of Transsexual Persons
Louis J. Gooren, M.D., Ph.D.

Long-Term Evaluation of Cross-Sex Hormone Treatment in Transsexual Persons
Katrien Wierckx, MD,∗ Sven Mueller, S.C., PhD,∗ Steven Weyers, MD, PhD,∗ Eva Van Caenegem, MD,∗ Great Roef, MD,∗ Gunter Heylens, MD, and Guy T Spoen, MD, PhD,∗

Care of Transsexual Persons
Louis J. Gooren, M.D., Ph.D.
5. Medications

a. Estrogens
b. Testosterone
c. (Anti-Androgens)
d. Progestins
e. GnRH Agonists (GnRH agonist),

Two Phases?

WHY?

Why not just initiate cross-gender Hormones?
Treatment Plan for Adolescents

**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

Why Two Phases?

Why not just initiate cross-gender Hormones?

**Outcomes**

**TRANS MEN**

**Dose Response Curve**

**ADULT PROTOCOL**

**TRANS MEN**

Testosterone Dose Response Curve

**NATAL WOMEN**

50  240  950

**Outcomes**

Dose
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

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 Dose Response Curve

ADULT PROTOCOL

MEN

TRANS WOMEN

NATAL MEN

TRANS WOMEN

Dose

Outcomes

50

240

950
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

Testosterone Suppression by Estradiol

Avg E2 = 96 pg/ml

Estradiol

135 pg/ml

#5 #6 #7 #8 #9 #10

Estradiol Testo LH

Testosterone Suppression by Estradiol

Estradiol Testo LH

#5 #6 #7 #8 #9 #10

<table>
<thead>
<tr>
<th>Protocol: Transition Male to Female</th>
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<tbody>
<tr>
<td>Phase 1 (OR Simultaneously)</td>
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<tr>
<td>Two–Three (12) Months Androgen Suppression</td>
</tr>
<tr>
<td>1. Cyproterone Acetate – 50 mg/day</td>
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<tr>
<td>2. Spironolactone <strong>100</strong> – 200 mg/day</td>
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<tr>
<td>3. GnRH Analog</td>
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<tr>
<td>4. Medroxyprogesterone + GnRH Agonist</td>
</tr>
<tr>
<td>Gradual Increase MP – 10-40 mg/day</td>
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<tr>
<td>GnRH Agonist Monthly x2</td>
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<tr>
<td>5. Finasteride - ? Anti-Androgen; Hair Loss</td>
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<tr>
<td>GOAL: Testosterone &lt; 50 ng/dl</td>
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**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**

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Progestins should be discontinued below the age of 40, estradiol valerate 4 mg daily is now recommended. After the age of 40, transdermal estrogens (17-β estradiol gel 2 mg daily or 17-β estradiol patch 100µg twice a week) is (SRS). In 1986, at the start of our multidisciplinary team, a dual-phase hormonal schedule After 6 months up to 1 year treatment with cyproterone acetate, cross-sex hormones were added [1]. Recently, we changed our hormonal protocol, and we now prescribe antiandrogens (mostly cyproterone acetate 50 mg) and estrogens simultaneously to the majority of transsexual women (male-to-female

Guy T’Sjoen, MD, PhD*6
**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

**Phase/Step One**

- Progesterone 20-60 mg PO daily
- Medroxyprogesterone acetate 150 mg IM every 3 months
- Cyproterone acetate 50-100 mg PO daily
- GnRH agonist (leuprolide) 3.75-7.5 mg IM monthly
- Histrelin implant 50mg implanted every 12 months
- Spironolactone 100-200 mg PO daily
- Finasteride 1 mg PO daily

**Phase/Step Two**

- Testosterone
- Estrogen
- Cortisol x10
- Prolactin
QUESTIONS