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

1. Mental Health Professionals

GENDER DYSPHORIA: COMPLEXITY

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

WHAT IS
GENDER DYSPHORIA?

NOT
GENDER IDENTITY DISORDER

NOT
TRANSSEXUALISM

NOT
GENDER NONCONFORMING PEOPLE

WHY DOES
GENDER DYSPHORIA
OCCUR?

Care of the transgender patient: the role of the gynecologist

Cécile A

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

Care of the transgender patient: the role of the gynecologist

Cécile A. Unger, MD, MPH American Journal of Obstetrics & Gynecology JANUARY 2014

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.

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.

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.

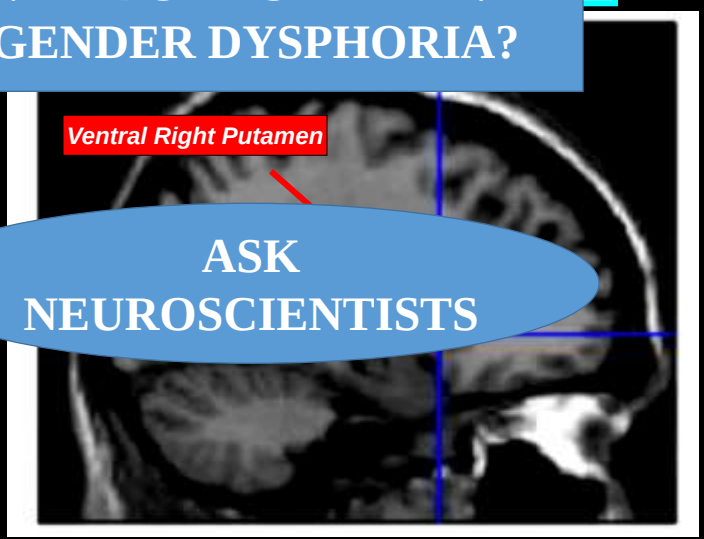
Differential Brain Processing of Audiovisual Sexual Stimuli in men: Comparison positron emission tomography study of the initiation and Mair
Miya

WHY DO PEOPLE HAVE GENDER DYSPHORIA?

rCBF

Regional Cerebral Blood Flo

Oxygen-15 Water Given During Pet Scan



ASK NEUROSCIENTISTS

Differential Brain Processing of Audiovisual Sexual Stimuli in men: Comparison positron emission tomography study of the initiation and Maintenance of penile erection during sexual arousal.
Miyagawa, et al. J.NeuroImage 2007; 3: 2-12.

rCBF

Regional
Cerebral
Blood
Flow

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Water
Given
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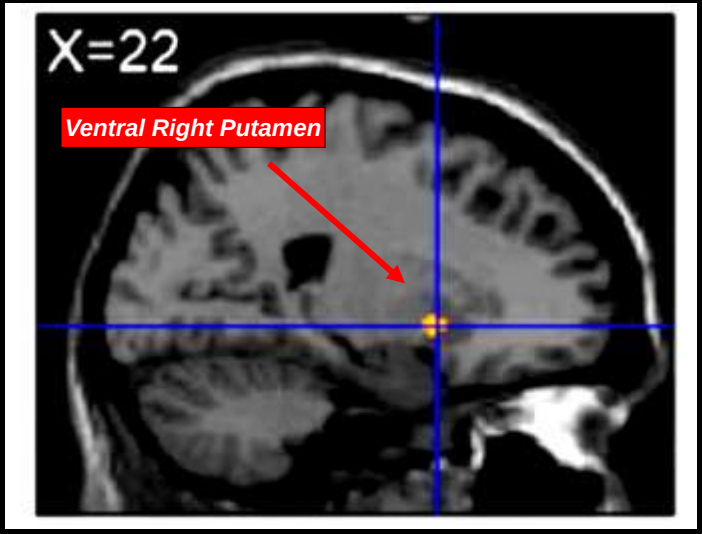
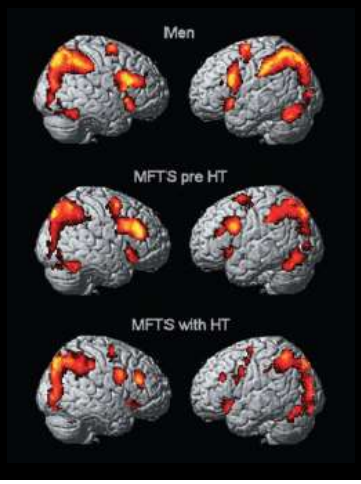
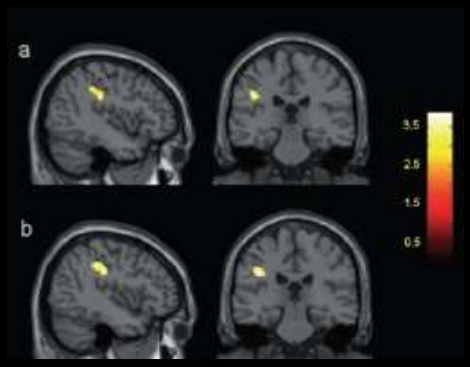


Neuroimaging Differences in Spatial Cognition between Men and Male-to-Female Transsexuals Before and During Hormone Therapy

J Sex Med 2010;7:1858–1867

Sonja Schöning, PhD,*† Almut Engelien, MD,*‡§ Christine Bauer,*† Harald Kugel, PhD,§ Anette Kersting, MD, PhD,* Cornelia Roestel, MD,* Pienie Zwitserlood, PhD,¶ Martin Pyka,*† Udo Dannlowski, MD,* Wolfgang Lehmann, PhD,** Walter Heindel, MD, PhD,§ Volker Arolt, MD, PhD,* and Carsten Konrad, MD*†‡

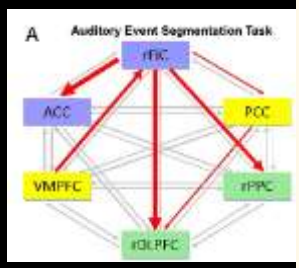




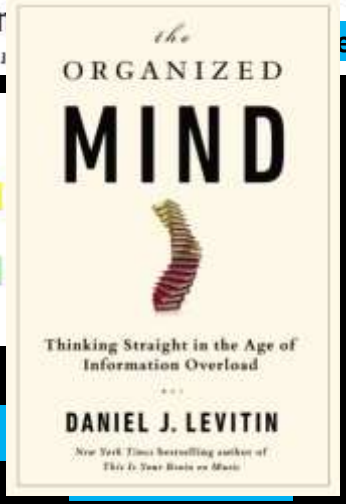
A critical role for the right fronto-insular cortex in switching between central-executive and default-mode r

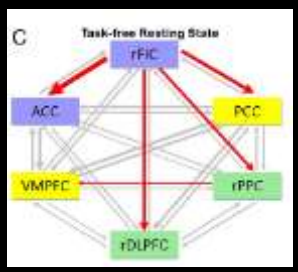
Devarajan Sridharan*[1], Daniel J

el Levitin



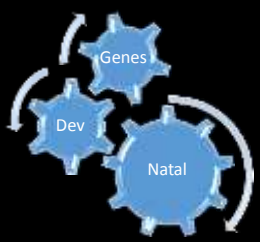
AUDITORY EVENT SEGMENTATION

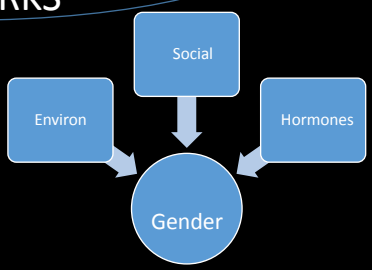


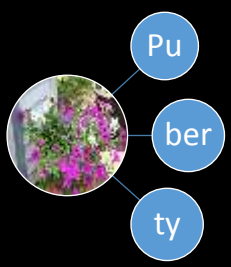


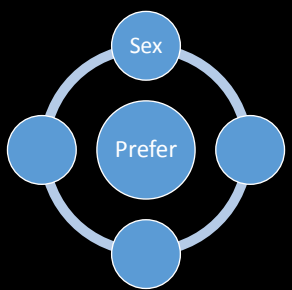
DEFAULT MODE

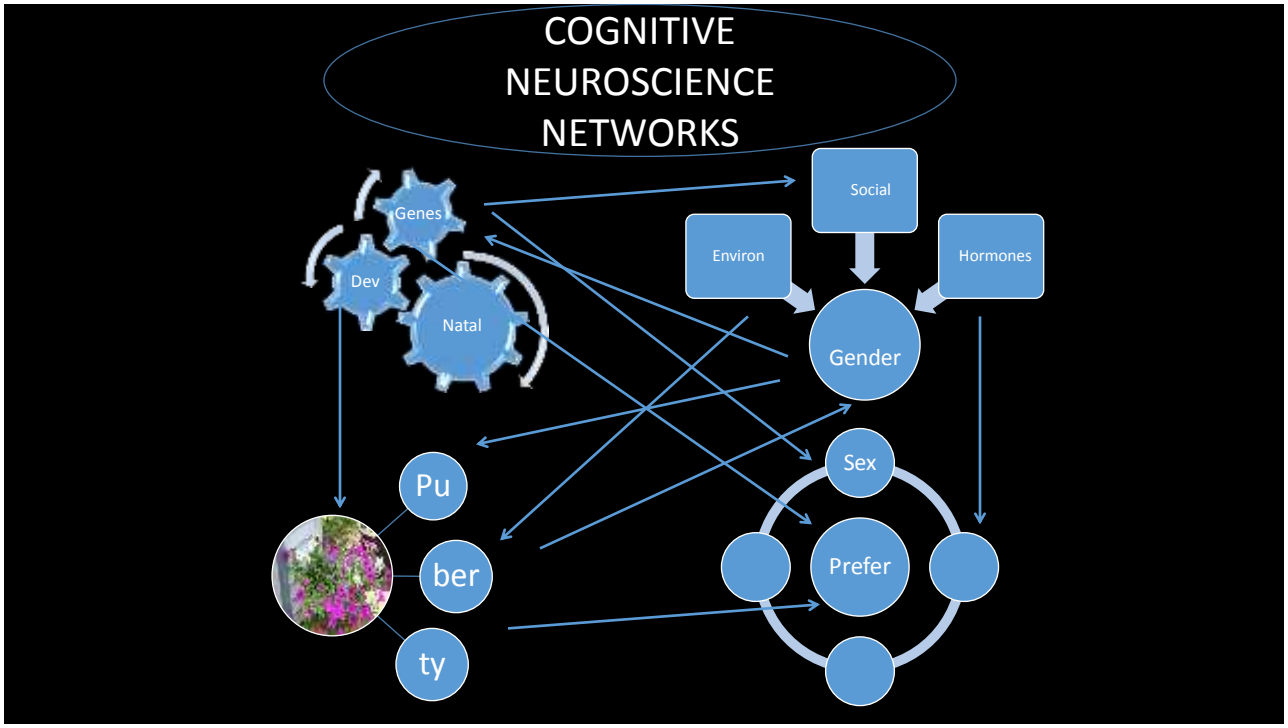
COGNITIVE NEUROSCIENCE NETWORKS











Care of the transgender patient: the role of the gynecologist

Cécile A.

GENDER DYSPHORIA: LESS COMPLEX

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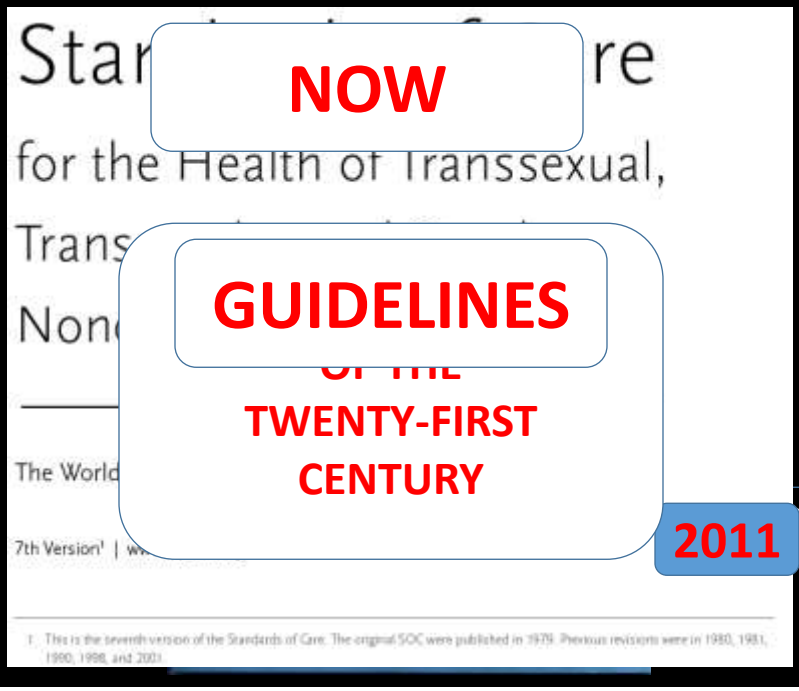
PROTOCOL
(Dutch, French, Greek)

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

(Endocr Pract. 2003;9:12-21)

Vin Tangpricha, MD,[1] Stanley H. Ducha... and Stuart R. Chipkin, MD, FACE[4]

2003

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

Dittrich R, et al Exp Clin Endocrinol Diabetes 113: 586-592, 2005

Erlangen, Germany

2005

Long-Term Administration of Testosterone Undecanoate

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,* Greet Roef, MD,* Gunter Heylens, MD,§ and Guy T'Sjoen, MD, PhD*§

2012

Care of Transsexual Persons

Louis J. Gooren, M.D., Ph.D.

1997-2011

5. Medications

a. Estrogens

ne

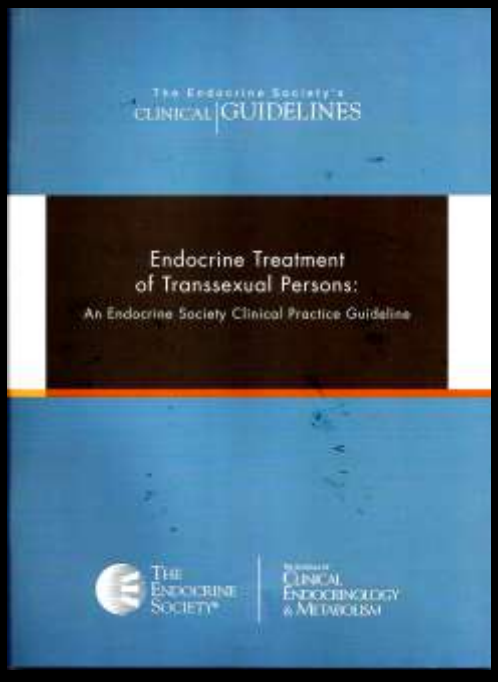
ogens)

(GnRH agonist),

nists

Antiandrogens
- Spironolactone
- Cyproterone acetate**
- Goserlin acetate
- Finasteride
- Dutasteride

Progestins
- Medroxyprogesterone
- Micronized progesterone


The Endocrine Society's
CLINICAL GUIDELINES
Endocrine Treatment
of Transsexual Persons:
An Endocrine Society Clinical Practice Guideline
THE ENDOCRINE SOCIETY
JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

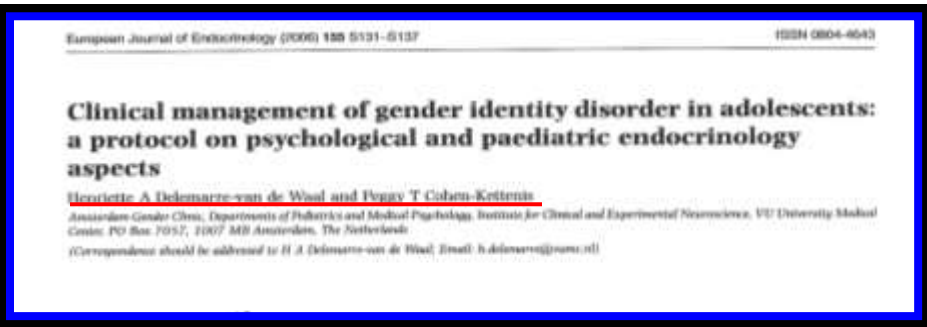
2009


Standards of Care
for the Health of Transsexual,
Transgender, and Gender
Nonconforming People
The World Professiona Association for Transgender Health
7th Version[1] | 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 1980, 1981, 1990, 1998, and 2001.

2011

Why Two Phases?

Why not just initiate cross-gender Hormones?



European Journal of Endocrinology (2006) 155 S131–S137 ISSN 0804-4643

Clinical management of gender identity disorder in adolescents: a protocol on psychological and paediatric endocrinology aspects

Henriette A Delemarre-van de Waal and Peggy T Cohen-Kettenis

Amsterdam Gender Clinic, Departments of Pediatrics and Medical Psychology, Institute for Clinical and Experimental Neuroscience, VU University Medical Center, PO Box 7057, 1007 MB Amsterdam, The Netherlands

(Correspondence should be addressed to H A Delemarre-van de Waal; Email: h.delemarre@vumc.nl)

Hormone Therapy for Adolescents

- Goal: Arrest pubertal development of unwanted characteristics of anatomic (natal) sex

GENDER DYSPHORIA: CONTROVERSY

Univ. of Toronto

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%

TRANS ADOLESCENTS

Why Two Phases?

Why not just initiate cross-gender Hormones?

Treatment Plan*

- Diagnostic evaluation
- PHASE ONE
- 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

Endocrine Treatment of Transsexual Persons: An Endocrine Society Clinical Practice Guideline

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

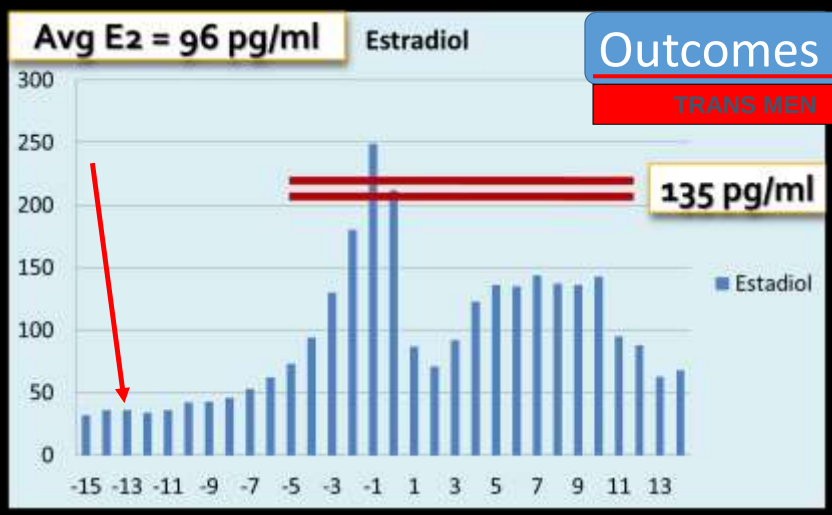
TRANS MEN

Why Two Phases?

Why not just initiate cross-gender Hormones?

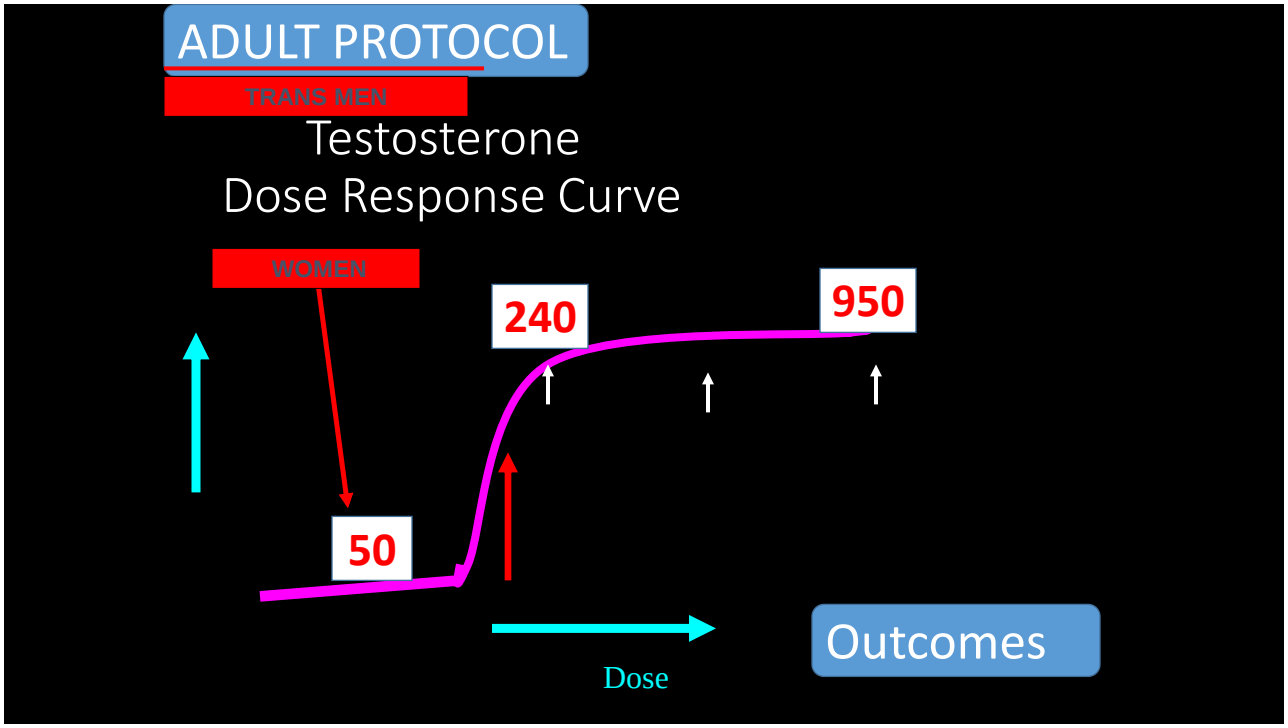
Establishment of detailed reference values for luteinizing hormone, follicle stimulating hormone, estradiol, and progesterone during different phases of the menstrual cycle on the Abbott ARCHITECT® analyzer

Clin Chem Lab Med 2006;44(7):883–887



Outcomes

TRANS MEN



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%

R. Dittrich*

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.

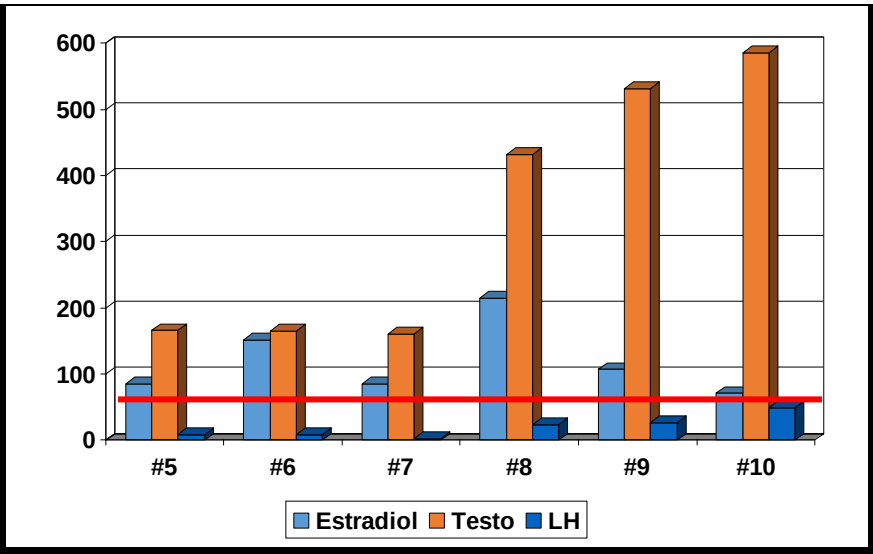
Wylie C. Hembree,

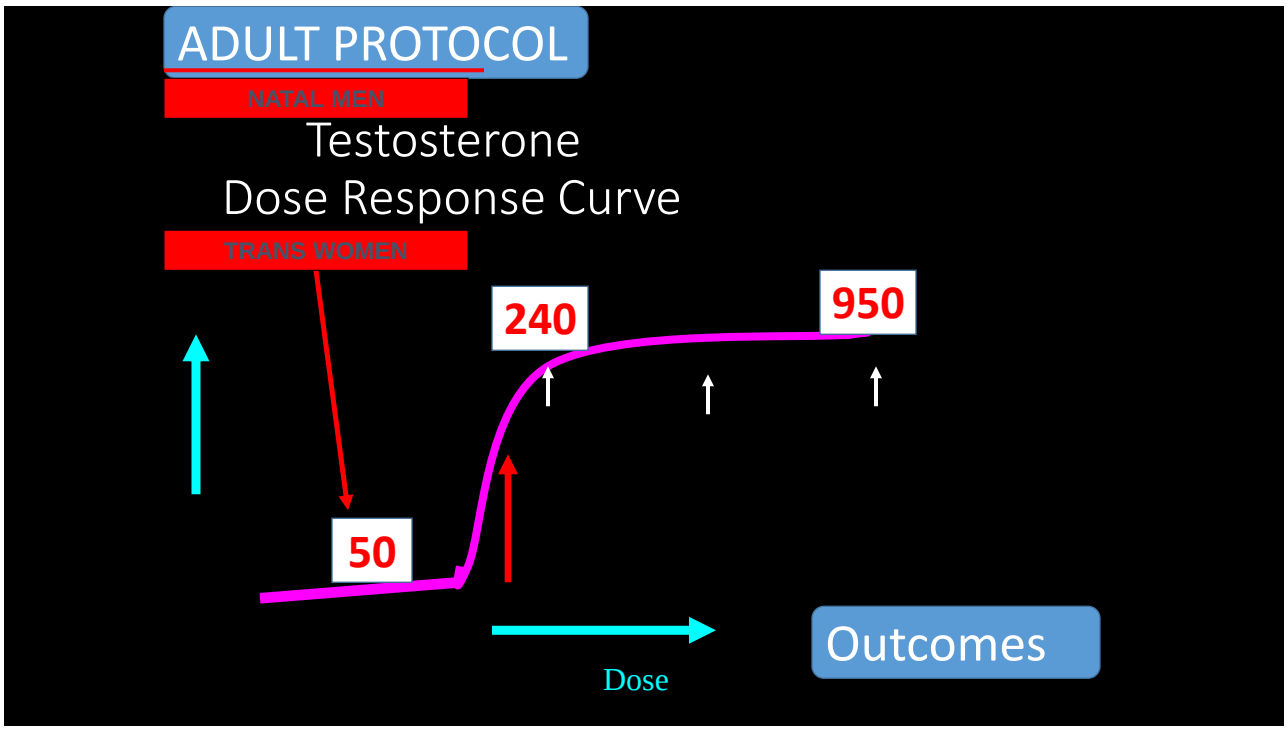
TRANS WOMEN

Why Two Phases?

Why not just initiate cross-gender Hormones?

Testosterone Suppression by Estradiol





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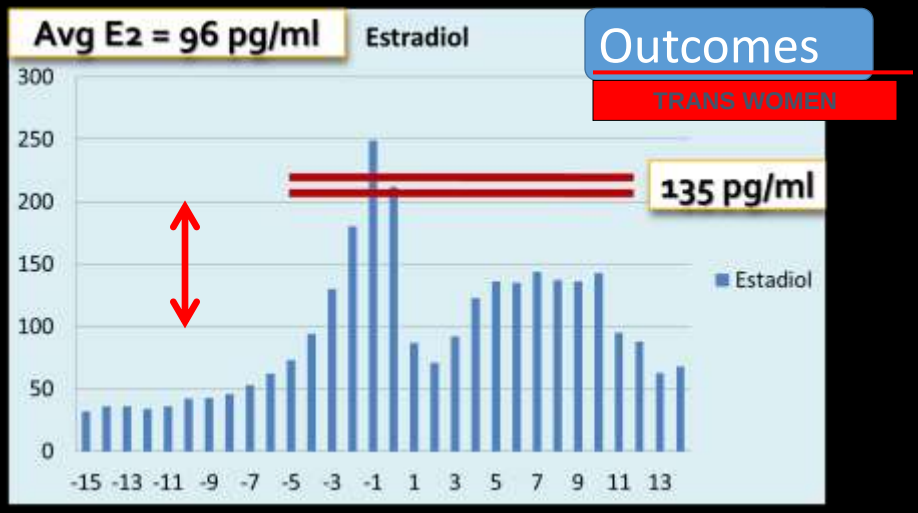


Protocol: Transition Male to Female

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

Louis J. Gooren, M.D., Ph.D.

Guy T'Sjoen, MD, PhD*§

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*§

Protocol: Transition Male to Female

1998 - 2013

Two – Three Months

Medroxyprogesterone

Gradual Increase MP – 10-40 mg/day

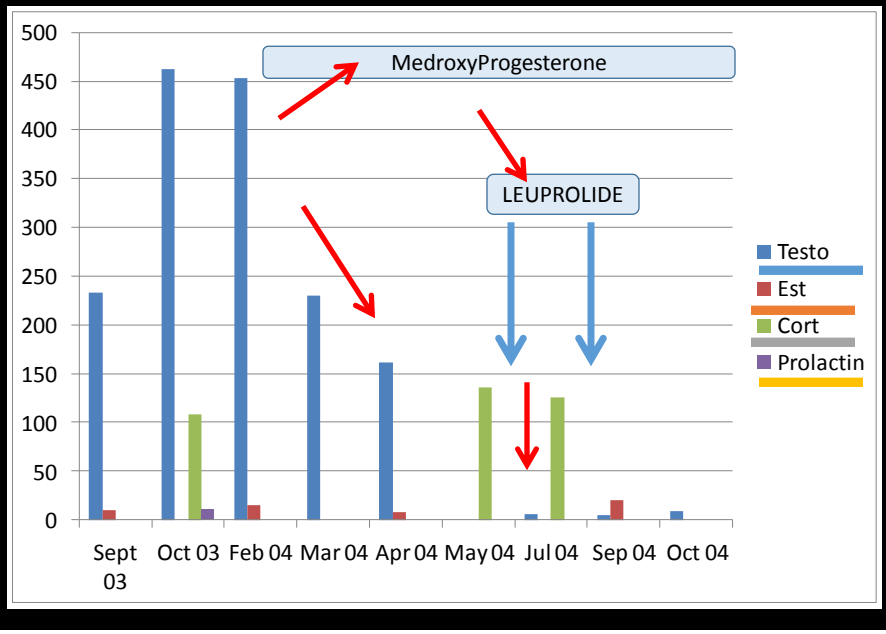
GnRHa x 2 months

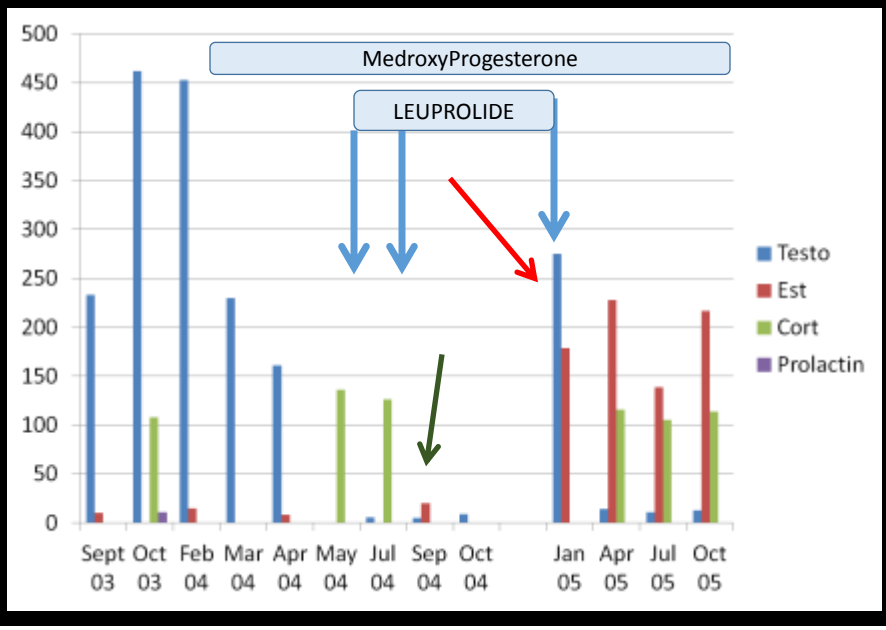
Gradual Addition of Estradiol

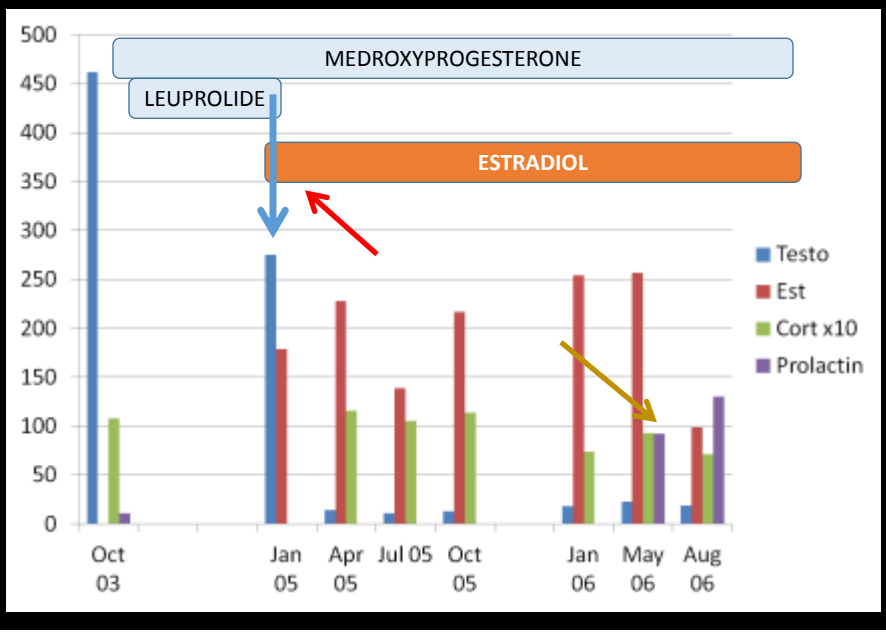
Oral, IM, Patches

Check LH and Testo 6-8 weeks

After GnRHa agonist




MedroxyProgesterone
LEUPROLIDE
500
450
400
350
300
250
200
150
100
50
0
Sept 03
Oct 03
Feb 04
Mar 04
Apr 04
May 04
Jul 04
Sep 04
Oct 04
Jan 05
Apr 05
Jul 05
Oct 05
Testo
Est
Cort
Prolactin


MEDROXYPROGESTERONE
LEUPROLIDE
ESTRADIOL
500
450
400
350
300
250
200
150
100
50
0
Oct 03
Jan 05
Apr 05
Jul 05
Oct 05
Jan 06
May 06
Aug 06
Testo
Est
Cort x10
Prolactin

PHASE/STEP TWO

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

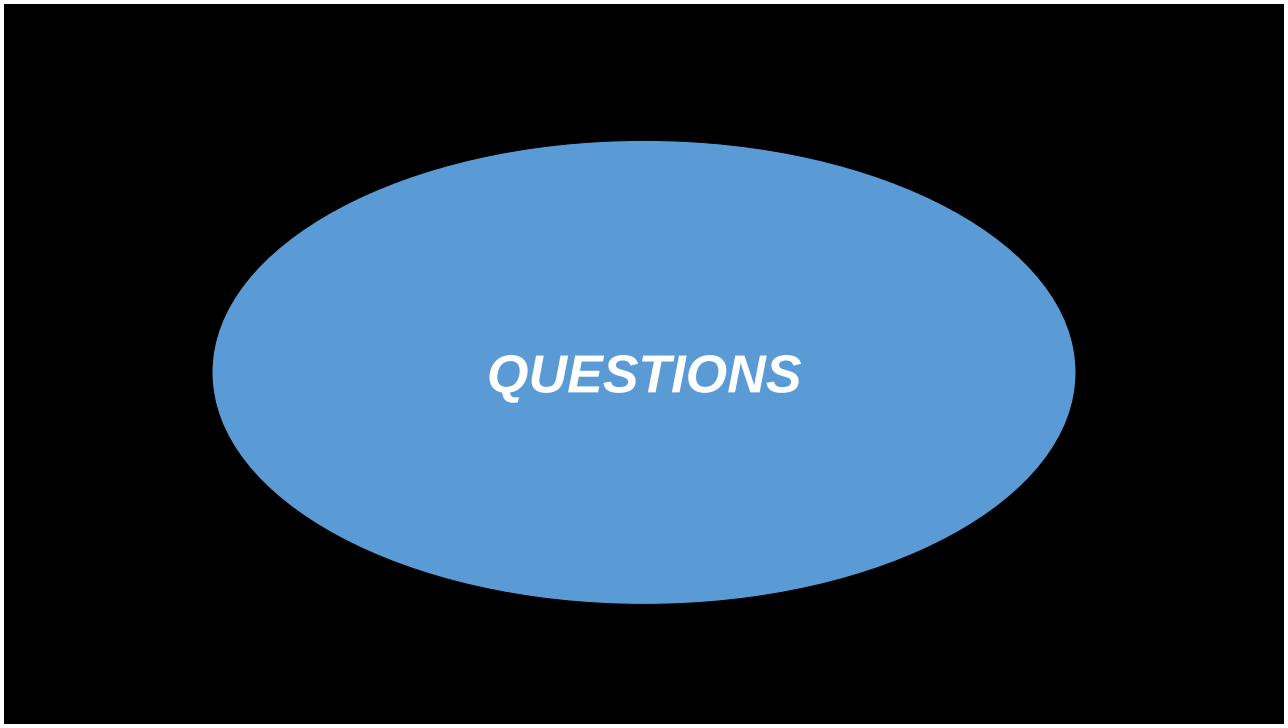
PHASE/STEP ONE

PROGESTINS GnRH ANALOGS

- Progesterone 20-60 mg PO daily
- Medroxyprogesterone acetate 150 mg IM every 3 months
- Cyproterone acetate 50-100 mg PO daily[a]
- 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

CONTROVERIES

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