ADULT TRANSGENDER MEDICINE: HORMONAL AND SURGICAL CONSIDERATIONS

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DISCLOSURE

- 3rd year Endocrine Fellow at UVA
- I will discuss off label use or investigational use in my presentation
- I don't have financial relationships to disclose

OBJECTIVES

- Prevalence
- Fertility
- Basics of Treatment/Monitoring
- Treatment concerns in chronic disease
- Surgical Options

PREVALENCE

- True prevalence is unknown, current data likely underestimate
- Western Countries:
  - Male to Female has ~2:1 predominance, ~1:10,000 MtF and ~1:30,000 FtM
  - In Asia, FtM more predominant ~1:2
- Some estimates ~1:250

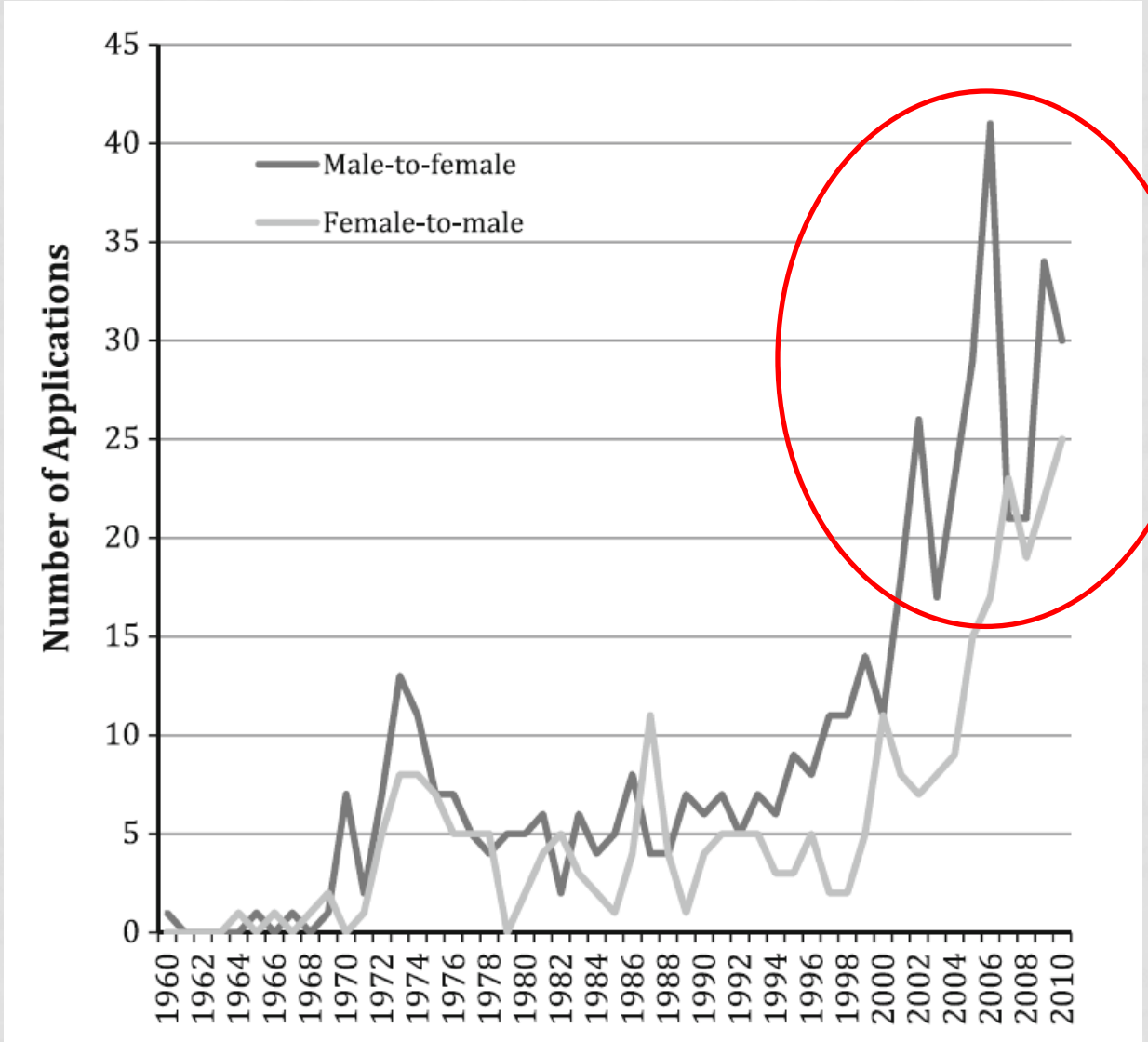
- HHS undergoing a survey to get better estimate

UVA EXPERIENCE 2015

- 23 initial visits in 6 months
- 60 active transgender patients (seen within last 2 years)
  - 21 Female to Male
  - 39 Male to Female
- 83% seen in fellows clinic (Monday or Friday AM)
- Average age: 39 years
  - 25% are age 50 or above

- Numbers are growing!

New applicants for Gender Reassignment Surgery in Sweden 1960-2010



Dhejne C et al. An Analysis of All Applications for Sex Reassignment Surgery in Sweden, 1960–2010: Prevalence, Incidence, and Regrets. Arch Sex Behav (2014) 43:1535–15

OBJECTIVES

- ~~Prevalence~~
- **Fertility**
- **Basics of Treatment/Monitoring**
  - Treatment concerns in chronic disease
  - Surgical Options

SOURCES

- Endocrine Society Guidelines on Transsexual Persons (2009)
- New Guidelines coming out soon

SPECIAL FEATURE

Clinical Practice Guideline

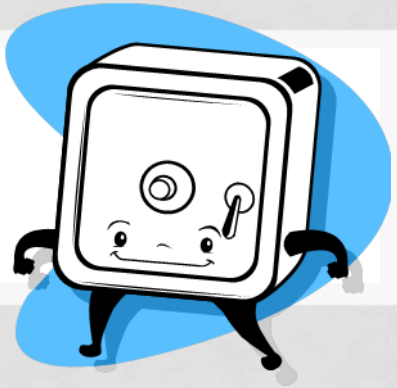
Endocrine Treatment of Transsexual Persons: An Endocrine Society Clinical Practice Guideline

Wylie C. Hembree, Peggy Cohen-Kettenis, Henriette A. Delemarre-van de Waal, Louis J. Gooren, Walter J. Meyer III, Norman P. Spack, Vin Tangpricha, and Victor M. Montori*

INITIAL VISIT BEFORE STARTING HORMONES

- Assess general health, comorbid conditions, list of all supplements
- Family history: clotting disorders, premature CAD, CVA
- Discuss expectations for hormone therapy and estimated timeline for physical changes
- Counsel on smoking cessation if necessary
- Consider referral to a medical health professional comfortable with making the diagnosis of gender dysphoria if needed
  - It may be useful to have an patient follow with a therapist throughout their transition but not mandatory
- Discuss fertility expectations

FERTILITY



- Fertility be affected by hormones
- Must discuss sperm or egg banking prior to starting on hormone replacement if desire biological children
  - Female to Male may be able to resume fertility/menstrual cycles after stopping testosterone but not guaranteed
  - Male to Female fertility will be affected
  - Sperm bank in Richmond and Dr. Ryan Smith at UVA will also assist with sperm banking

MONITORING FOR ALL

- Typically labs done every 3 months for the first year
- Yearly (or twice yearly) monitoring after that

- Labs checked: CBC, Lipids, Estradiol, Testosterone, CMP
  - in various combinations

FEMALE TO MALE (FTM) TRANSGENDER

- Testosterone therapy
- Can be given as IM (or subcut) injections weekly or biweekly
  - If weekly, average dose 40-50mg
  - If biweekly, average dose 100mg
- Topical preparations (gel or patches) once daily
  - Usually 5mg packet or patch daily
- Most use IM/subcut injections due to cost
  - FYI: Subcut T not FDA approved

PHYSICAL CHANGES: FTM

- Early changes (3 months):
  - cessation of menses
  - increased libido
  - increased oiliness of skin, acne
- Later changes (6 months-1 year):
  - increased muscle mass
  - redistribution of fat mass
  - increased facial and body hair
  - deepening of the voice
  - clitoromegaly
  - maybe male pattern hair loss
- Maximum changes usually after 4 years of continuous therapy—most patients satisfied with cosmetic effect and can easily "pass" as biologic male

MONITORING

- Goal is T in mid-normal range (500s-600s ng/dl)
- If using gel: check levels about 1 month after a new dose
- If using injections:
  - Weekly: check mid-week injection level (3-4 days after injection) Biweekly: need to check 2 levels
    - A peak level 3-4 days after injection (level high end of normal: 800-1000ng/dL)
    - A trough level 3-4 days before next injection (level should be low normal 300s-400s mg/dL)
- Most end up preferring weekly injections because levels are more constant
  - With larger biweekly doses: mood lability (increased irritation, quick to anger), bothersome libido 2-3 days after injection with fatigue/depression towards the end of the 2 weeks

MALE TO FEMALE (MTF) TRANSGENDER

- 2 main components: estrogen and an anti-androgen
  - Sometimes add progesterone (rarely)
- Estrogens (specifically estradiol)
  - Patch twice weekly (preferred): 0.1mg-0.4mg
    - May have issues with adhesive (rash, itching)
    - Can swim, shower, etc with patch
  - Oral/sublingual pill daily: 2mg-6mg daily
  - IM injections weekly: 4-6mg weekly
- Goal: estrogen levels in mean female range (~150-200) with suppressed testosterone levels

MALE TO FEMALE: ANTI-ANDROGENS

- Spironolactone
  - 50-100mg twice daily
  - Blocks effects of androgens at the level of the hair follicle
    - Close monitoring in CKD due to hyperkalemia
    - Monitor BP
- Finasteride
  - 5-alpha reductase inhibitor
  - 5mg daily
  - Not my first choice
    - Hypotension
    - May have sexual side effects (decreased libido)
    - Less effective
  - May be helpful add-on for male-pattern baldness

PHYSICAL CHANGES: MTF

- Earlier changes (3-6 months):
  - decreased libido, often suppression of erections
  - decreased oiliness of skin
  - breast tissue growth
  - redistribution of fat mass
- Later changes (2-3 years):
  - breast development complete,
  - hair growth on face and arms/legs decreases (but unlikely to fully resolve)
  - Decrease testicular volume and sperm count
- Estrogen dose does not determine breast size
- Voice pitch does not change

MALE TO FEMALE: PROGESTERONE

- Current guidelines don't recommend adding progesterone until 2 years of estrogen therapy due to risk of inhibiting breast development
  - Data based on breast development in adolescent girls, unclear if valid for transgender individuals
- Will help suppress testosterone if still needed despite adequate estradiol levels
- No role for "cyclic" dosing of progesterone
- Is also thrombotic and sedating
- Belief by patients that progesterone is more "feminizing"

OBJECTIVES

- ~~Prevalence~~
- ~~Fertility~~
- ~~Basics of Treatment/Monitoring~~
- **Treatment concerns in chronic disease**
- Surgical Options

LONGITUDINAL RESEARCH

- 100 individuals (all who had gender surgery), average follow-up 11.3 years on hormones
- 25% of MtF women had osteoporosis at the lumbar spine and radius

- 6% of MtF had a thromboembolic event
- 6% of MtF experienced other cardiovascular problems
- HOWEVER, all individuals who had events were current smokers except 1 who was a former (18yr PDD) smoker and ALL were on oral ethinyl estradiol

- Wierckx K, Mueller, S, Weyers S, Van Caenegem E, Roef G, Heylens G, and T'Sjoen G. Long-term evaluation of cross-sex hormone treatment in transsexual persons. J Sex Med 2012;9:2641–2651.

LONGITUDINAL RESEARCH

- 966 male-to-female (MtF) and 365 female-to-male (FtM)
- Average length of follow-up 18.5 years (110 on hormones >30 yrs)
- 35% current and 35% former smokers
- MtF:
  - Risk increased 3-fold for current use of ethinyl estradiol increased CAD and CVD mortality but not other estrogen preparations
  - 28 deaths due to cancer, not increased compared to general population
- FtM: No increased death or events in FtM compared to general population

- Asscheman H., Giltay E.J., Megens J.A.J., de Ronde W., van Trotsenburg M.A.A., and Gooren L.J.G.: A long-term follow-up study of mortality in transsexuals receiving treatement with cross-sex hormones. Eur J Endocrinol 2011; 164: pp. 635-642

RISKS OF ESTROGEN

- Increased risk of blood clots
  - Most endocrinologists will not start estrogens if patient is smoking
  - Concern if has clotting disorder
  - Patches avoid first pass metabolism and may be minimize the risk of clots
- Severe migraine headaches
- Elevated prolactin levels (0-70% depending on study)
- Coronary artery disease (?)
- Cerebrovascular disease (?)
- Liver dysfunction and increase Triglycerides
- Breast cancer (?)

RISKS OF TESTOSTERONE

- **Erythrocytosis (Hemoglobin/Hematocrit >16/40)**
- **Liver dysfunction (transaminases > 3 x upper limit of normal)**

- **Breast or uterine cancer (?)**
- **Does NOT appear to be increased risk of CAD**

- **Monitor Lipids, CBC, CMP**

Wierckx K et. al Long-Term Evaluation of Cross-Sex Hormone Treatment in Transsexual Persons. Journal of Sexual Medicine. 2012;9:2641–265

OBJECTIVES

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- **Surgical Options**

SURGICAL POSSIBILITIES

- Most patients do not undergo surgery
- Depending on surgeon, will require individual to be taking hormones at least 1 year
- Most common surgery is “top” surgery or mastectomy for Female to Male
- Gender confirmation surgery (aka gender reassignment surgery) less common due to:
  - Expense
  - Lack of insurance coverage
  - Patient preference
  - Surgical complications and outcomes

GENDER REASSIGNMENT SURGERY

- "Gender Confirmation Surgery"
- MTF: vaginoplasty, clitoroplasty, labioplasty
- FTM: penile-scrotal reconstruction

- Male to Female may also consider:
  - Facial feminization
  - Feminization laryngoplasty

GENDER REASSIGNMENT SURGERY: MTF

- Bowel segment vaginoplasty--new
  - 1st choice if puberty previously arrested
  - Secondary vaginoplasty if corrections needed
- Advantages: length, texture and appearance similar to a natural vagina, and natural lubrication
- Disadvantages: diversion colitis, excessive mucus production, stenosis, ulcerative colitis, peritonitis, intestinal obstruction and junctional neuroma

GENDER REASSIGNMENT SURGERY: MTF

- Clitoroplasty: using the glans from the neurovascular bundle, which lies between Buck's fascia and the corpora cavernosa
  - Sexual satisfaction achieve in 98% of cases
- Labia majora constructed from scrotal skin
- Labia minora: limited techniques, use penile skin if available

GENDER REASSIGNMENT SURGERY: FTM

- Phalloplasty: Harvest flaps from forearm, fibula, thigh or latissimus dorsi muscle
- High complication rates
  - Major surgery
  - Urinary fistulas in 20-40% (50% require surgical revision)
  - Urinary strictures: 25-60% of patients
  - Extensive recovery time (3 weeks inpatient)
  - Requires implantation of hydraulic erectile prosthesis—very high complication rate
  - Post-urinary dribbling in ~80%
  - Overall Revision rate is 40%

GENDER REASSIGNMENT SURGERY: FTM

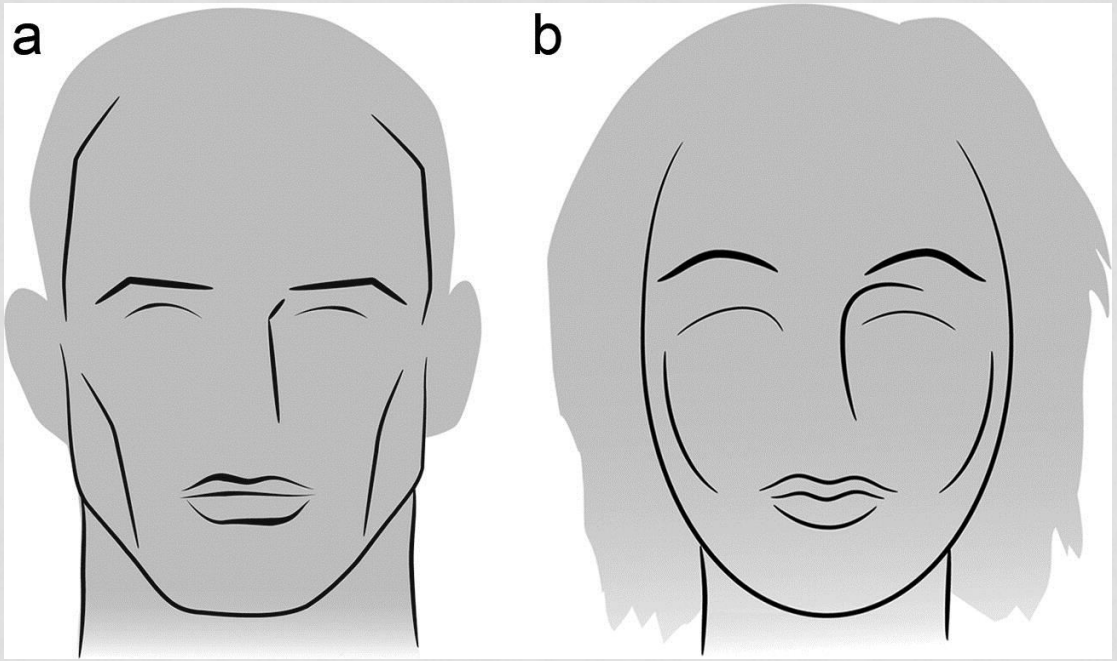
TABLE 1: Benefits and Limitations of Phalloplasty Surgical Techniques

Surgical Technique	Benefits	Limitations
Free flap		
Radial forearm flap	Possibly best cosmetic and functional result	Urinary tract complications, multiple stages, donor site morbidity, prosthesis
Thigh flap	Easy to hide donor site	Similar to radial forearm, no long-term data
Fibula flap	No need for erection device	Urinary tract not reconstructed, muscle and erection function and sexual and tactile sensitivity questionable, no long-term data
Latissimus dorsi flap	No need for erection device	Urinary tract not reconstructed, muscle and erection function and sexual and tactile sensitivity questionable, no long-term data
Suprapubic flap	Ease of technique	Poor cosmetic result, donor site morbidity, urinary tract problems, poor sensation, multiple stages
Other		
Metoidioplasty	Easy technique, reduced complications, quick recovery time	Short phallus, not capable of sexual penetration, cannot void while standing

Blaschke E et al. Postoperative imaging of phalloplasties and their complications. American Journal of Roentgenology. 203(2):323-8, 2014 Aug.

FACIAL FEMINIZATION

- Can include:
  - Forehead reduction
  - Hairline correction by scalp advance
  - Brow lift
  - Rhinoplasty
  - Cheek implants
  - Lip lift
  - Genioplasty (chin shaping)
  - Angle shave and taper of jaw
  - "Thyroid shave" (shaping of laryngeal prominence)
  - Price tag: ~$50,000



Altman K. Facial Feminization: Current state of the art. International Journal of Oral & Maxillofacial Surgery. 41(8):885-94, 2012 Aug.

THANK YOU!

- ~~UVA statistics~~
- ~~Fertility~~
- ~~Basics of Treatment/Monitoring~~
- ~~Treatment concerns in chronic disease~~
- ~~Surgical Options~~

Special thanks to Drs.
Chris McCartney and
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