FENWAY HEALTH

Fertility Issues for Transgender Persons

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Fenway Health

Transgender

- refers to a person who is born with the genetic traits of one gender but has the internalized identity of another gender

- The goal of treatment for transgender people is to improve their quality of life by facilitating their transition to a physical state that more closely represents their sense of themselves.

Transgender Demographics

- Massachusetts Behavioral Risk Factor Surveillance Survey (2007, 2009)
  - 0.5% of population between ages 18-64
- California LGBT Tobacco Survey
  - 0.1% of adult population
- Estimate in U.S. from the Williams Institute
  - 0.3% of adults
  - Approximately 700,000 people

Etiology of Transgender

- Research into genetics, brain anatomy and function, hormonal influences, but, the fact is, we just don't know.

- Recent review of twin studies shows an approximate 30% concordance in MtF monozygotic twins and an approximate 23% concordance in FtM monozygotic twins (Diamond, 2013)

Gender Dysphoria

- 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 secondary sex characteristics) Coleman, SOC, V 7 p168
- The focus of health care engagement is alleviating the distress.

Transgender Standards of Care

Advances in Treating Gender Dysphoria

- Increasingly standards of care are focused on individualized approaches to alleviate gender dysphoria.
- Approaches use various combinations of psychotherapy, hormone therapy and surgery to overcome gender dysphoria

Female to Male Treatment Options

- **Injectable Testosterone**
  - Testosterone Enanthate or Cypionate 100-200 mg IM q 2 wks (20 -22g x 1 ½" needles)
- **Transdermal Testosterone**
  - Androderm TTS 2-8mg daily
- **Topical testosterone**
  - Gels in packets and pumps, multiple formulations (Testim, Androgel) 5 to 10 gm applied topically daily
  - Axiron 2% pump gel for axillary application 1 pump to each axilla daily
- **Testosterone Pellet**
  - Testopel- implant 6-10 pellets q 3 to 6 months
- **Buccal Testosterone**
  - Striant 30 mg buccal system q 12 hours

Masculinizing Effects of Testosterone

Effect	Onset (months)	Maximum (years)
Skin oiliness/acne	1-6	1-2
Fat redistribution	1-6	2-5
Cessation of Menses	2-6	
Clitoral enlargement	3-6	1-2
Vaginal atrophy	3-6	1-2
Emotional changes		
Increased sex drive		

Masculinizing Effects of Testosterone

Effect	Onset (months)	Maximum (years)
Deepening of voice	3-12	1-2
Facial/Body Hair Growth	6-12	4-5
Scalp Hair Loss	6-12	
Increased Muscle Mass & Strength	6-12	2-5
Coarser Skin/ Increased Sweating		
Weight Gain/Fluid Retention		
Mild Breast Atrophy		
Weakening of Tendons		

Risks of Testosterone Therapy

- Lower HDL
- Elevated triglycerides
- Increased homocysteine levels
- Polycythemia
- Unknown effects on breast, endometrial, ovarian tissues
- Increased risk of sleep apnea
- (Insulin resistance)
- Hepatotoxicity ?
- Chronic pelvic pain
- Infertility

Male to Female Treatment Options

- **Antiandrogens**
  - Spironolactone (aldactone) 50-400mg PO daily (can be divided into BID dosing)
  - Finasteride (Proscar) 2.5-5mg PO daily
- **Oral Estrogens**
  - Estradiol (estrace) 2-6mg PO or SL daily(can be divided into BID dosing)
  - Premarin (conjugated estrogens) 1.25-10mg PO daily (can be divided into BID dosing)
- **Transdermal Estrogens**
  - Estradiol patch 0.1-0.4mg twice weekly
- **Injectable Estrogens**
  - Estradiol valerate 5-20mg IM q2 weeks
  - Estradiol cypionate 2-10mg IM weekly

Male to Female Treatment Options

- Cyproterone Acetate (not available in US)
- GnRH agonist: Goserelin Acetate
- Progestins: ??? Benefit on breast development, mood and libido, but associated with increased risk of cardiovascular events and breast cancer in WHI
  - Depo-Provera 150 mg IM q 3 months
  - Provera 2.5 to 10 mg PO daily*
  - Prometrium 100 mg – 200 mg po daily*
- * Consider dosing 10 days each month cyclically with po form to minimize risk

Feminizing effects of Estrogens & Antiandrogens

Effect	Onset (months)	Maximum (months)
Decreased Libido	1-3	3-6
Decreased Spontaneous Erections		
Breast Growth	3-6	24-36
Decreased Testicular Volume	3-6	24-36
Decreased Sperm Production	Unknown	Unknown
Redistribution of Body Fat	3-6	24-36
Decrease in Muscle Mass	3-6	12-24
Softening of Skin	3-6	Unknown
Decreased Terminal Hair	6-12	>36

NOTE:
•Possible slowing or cessation of scalp hair loss, but no regrowth
•No change in voice

Risks of Estrogen Therapy

- Venous thrombosis/thromboembolism
- Increased risk of cardiovascular disease
- Weight gain
- Decreased libido
- Hypertriglyceridemia
- Elevated blood pressure
- Decreased glucose tolerance
- Gallbladder disease
- Benign pituitary prolactinoma
- Breast cancer(?)
- Infertility

Endometrial changes on testosterone

Futterweit, et al (1986): 9/19 FtM patients had proliferative endometrium at the time of hysterectomy; 3/19 had endometrial hyperplasia.

Perrone, et al (2009): 27 FtM undergoing endometrial bx; all had atrophic endometrium similar to menopausal controls.

Urban, Teng & Kapp (2010): First case report of endomtrial carcinoma in an FtM patient after 7 years on testosterone tx.

Ovarian changes on testosterone

- Compared with controls, the FTM group had a thicker ovarian cortex (P = 0.0001), and more hyperplastic collagen (P = 0.001), ovarian stromal hyperplasia (P = 0.003) and stromal luteinization
- The number of primordial follicles was similar in the two groups (P = 0.22).
- The numbers of early stage (primary, pre-antral and early antral) follicles, which are dependent on androgen, were also similar (P = 0.81), as were the numbers of antral follicles (P = 0.97).
- In contrast, significantly greater numbers of atretic follicles were seen in the FTM than that in the control group (P = 0.01).

Ikeda, et al, 2012

Effects of testosterone on reproductive organs

- Pelvic pain in transmen
  - Investigate: organic cause, then consider: IBS, IC, Endometriosis, Depression/ Anxiety, Pelvic Floor Muscle
- ? Effect of testosterone on pelvic floor muscles

- Atrophic vaginitis

Effects of feminizing therapy on testes

108 patients, mean age 42 yo

- Complete spermatogenesis 24%
- Meiotic arrest 35%
- Spermatogonial arrest 35%
- Sertoli-cell only in 15%
- Tubular shadows in 2%

- 45.45 % of patients who stopped estrogen 6 weeks prior to SRS showed complete spermatogenesis
- 14.3% of those who continued CSHT up to surgery

(Schneider, et al, 2015)

Fertility in transwomen

2002 survey of trans women (De Sutter, et al)

- 77% said that the option to freeze sperm should be discussed and offered prior to CSHT
- 51% said they would have seriously considered banking sperm if it had been offered
- 90% said that fertility loss was not an important reason to defer hormonal transition

Wierckx (2012) noted that only 15% of trans women actually chose to bank sperm

Fertility in transwomen

27 transwomen, mean age 28.9 years

- 27.6% oligospermia
- 31% asthenozoospermia
- 31% tearatozoospermia

- Mean sperm concentration 46 million/ml
- Mean per cent mobility 42.9%

Fertility in Transmen

Weirckx , et al, 2012:

- More than half of trans men surveyed expressed a desire to have children
- 37.5 % would have preserved oocytes if it had been possible

Fertility in transgender persons

Transgenderism and reproduction

Guy T'Sjoena,b, Eva Van Caenegema, and Katrien Wierckxa

Current opinion in endocrinology, diabetes, and obesity, Dec 2013

Briefly mentions Thomas Beattie's pregnancy in 2008, but speaks mostly to the option of gamete banking/preservation

Traditional stance of advocating for gamete preservation prior to initiating hormone therapy

Fertility in Transmen

Transgender Men Who Experienced Pregnancy After Female-to-Male Gender Transitioning

- Alexis D. Light, MD, MPH, Juno Obedin-Maliver, MD, MPH, Jae M. Sevelius, PhD, and Jennifer L. Kerns, MD, MPH
- OBSTETRICS & GYNECOLOGY, VOL. 124, NO. 6, DECEMBER 2014

Fertility in Transmen

- 41 respondents who identified as trans-masculine
- 51% identifies as “male”
- Average age 28
- Predominantly white, well educated and well off
- 25 (61%) had used testosterone prior to pregnancy- 5 of them for more than 10 years!
- 28 (68%) were planned pregnancy (76% of those using T)
- Most were using condoms or no contraception prior
- 36 used own eggs, 4 eggs donated by “spouse”, 1 donor
- Sperm from “spouse” 76%, known donor 10%
- 7% used fertility drugs, 12% assisted reproduction

Fertility in Transmen

- Time to conception:
  - Unplanned 32% (6 guys on testosterone)
  - Less than 1 month 17%
  - 1-3 months 22%
  - 4-6 months 19%
  - more than 7 months 10%
  - Only 4% of guys who were on testosterone took longer than 3 months to conceive

Effects of Testosterone on the Fetus?

- In animals, early testosterone exposure causes disorders in development of sexual organs in female fetuses and also differences in play behavior and sexual response behavior
- In animals, effect on fetal growth and litter size
- Studies on girls with CAH and boys with CAIS suggest that fetal testosterone levels influence gendered play behavior and, to a lesser extent, sexual orientation and possibly gender identity
- Studies looking at maternal and amniotic fluid levels of testosterone have shown mixed results
- ? Higher androgen levels associated with autism and other psychopathology

Pregnancy

- Light, et al reported essentially normal pregnancies and no significant effect of previous testosterone use on pregnancy outcomes
  - Hypertension 12%
  - Preterm labor 10%
  - Placental abruption 10%
  - Anemia 7%

Pregnancy

- 9/25 (36%) patients who had previously been on testosterone had Cesarean section, but 3 of these patients elected to deliver surgically
- 3/16 (19%) of patients without prior testosterone delivered by Cesarean section

Pregnancy

- Loneliness and sense of isolation
- Varying degrees of gender dysphoria
- ? Higher risk of post-partum depression
  - McDonald, et al: 7 of 22 reported post-partum depression, 2 requiring medical treatment

Fertility in transgender persons

- One of the biggest issues in treating transgender adolescents relates to decisions around future fertility
- “Puberty Blockers” (GnRH agonists) will prevent the development of secondary sexual characteristics, including maturation of the gonads.
- It is possible that, after 2 to 3 years on puberty blockers, the individual could stop GnRH agonist and allow the anatomic puberty to occur in order to stimulate gonadal development and then bank gametes or consider later conception/pregnancy
- But most adolescents who start on GnRH agonists will go on to take cross-sex hormone therapy to masculinize or feminize body; this will permanently impair gamete development and fertility
- Some discussion around preserving immature testicular or ovarian tissue that can later be treated in vitro to stimulate gamete maturation, but not yet being done, ? potential for success