

Initial Evaluation

- Baseline history and counseling
 - Mood status (PHQ-9, GAD6, Mood Disorder Questionnaire)
 - Suicidal ideation
 - Smoking status & other VTE/hypercoagulable risk factors
 - Desire for fertility – counsel on fertility options
- Set **expectations** for what changes to expect from GAT (reference)
 - Body fat redistribution; 3-6 months; 2-5 years
 - Decreased muscle mass/strength; 3-6 months; 1-2 years
 - Softening of skin/decreased oiliness; 3-6 months; unknown
 - Decreased libido; 1-3 months; 3-6 months
 - Decreased spontaneous erections; 1-3 months; 3-6 months
 - Male sexual dysfunction; variable; variable
 - Breast Growth; 3-6 months; 2-3 years
 - Decreased testicular volume; 3-6 months; 2-3 years
 - Decreased sperm production; variable; variable
 - Thinning and slowed growth of body and facial hair; 6-12 months; >3 years
 - Male pattern baldness; no regrowth, loss tops 1-3 months; 1-2 years
- Absolute Contraindications: any active estrogen-sensitive cancer
- Complete Informed Consent Form & Upload to patient chart
- Enroll patient in Gender Affirming Therapy in the Clinic Navigator

Therapeutic Options

Estrogen – administer FIRST [36]

- Bioidentical Estradiol Oral/Sublingual (*most typical*)
 - Initial: 2-4 mg/day
 - Maximum: 8 mg/day (BID dosing if >2 mg daily)
- Others:
 - Estradiol Transdermal (lower or absent clotting risk [35])
 - Initial 100 mcg per [timing brand/product-dependent]
 - Maximum 100-400 mcg per timing brand/product
 - Estradiol valerate IM: Initial 20 mg IM q 2wk; Max 40mg IM q 2wk
 - Estradiol cypionate IM: Initial 2 mg IM q 2wk; Max 5 mg IM q 2 wk
 - Note: Conjugated equine estrogens (Premarin) are no longer recommended due to high risk of thrombogenicity and cardiovascular risk [38,39]

Androgen Blocker – Administer SECOND [32,36] –

- Spironolactone: Initial: 50 mg BID, Max: 200 mg BID

Optional Adjuncts (for reference)

- Finasteride 1-5 mg/day depending on desired effect
- Dutasteride 0.5 mg/day
- Progestagen
 - Micronized progesterone 100-200 mg/night
 - Medroxyprogesterone acetate (Provera), *less preferred*
 - Initial 2.5 mg/night; Max 10 mg/night

Estrogen Treatment Risks

Venous Thromboembolism

- VTE background rate in general pop: (1/1,000-1/10,000)
- Data on risk of oral 17-Beta estradiol (bioidentical) is MIXED – Some = no increased risk [49]
 - Some = 2.5-4 fold increase in relative risk (still low absolute risk) [50,51]
- Often quoted study: [52,53] Found 20-40-fold times risk of VTE in transgender women, BUT:
 - 1) high doses (100-200 mcg/day)
 - 2) thrombogenic ethinyl estradiol (conjugated) used and
 - 3) Mix of smokers and non-smokers in cohort
- Routine hypercoagulability screening is not recommended
- Withhold estrogen therapy when: 1) patients with significant risk factors/history of VTE and 2) who continue to smoke tobacco
- If risks are great, but manageable—consider transdermal estrogen application

Loss of erectile function

- Some do not lose, can be safely preserved with Viagra or Cialis

Libido loss

- 22% met criteria for Hypoactive Sexual Desire Disorder (HSDD), no correlation with testosterone levels [59]
- Mental health therapy – continue throughout treatment to help with body image issues and dissociative symptoms

Prolactinoma [56]

- Few case reports reporting association with estrogen therapy
- Prolactin levels should only be checked in cases of
 - Visual disturbance, Excessive galactorrhea, New onset headaches

Migraine

- Estrogen known association with menstrual migraines (by period cycle in non-transgender women)
- May be exacerbated with feminizing GAT

Infertility

- Sperm cryopreservation may be required

Labs Baseline & Prior to Every Visit

- Serum Estradiol (NOT TOTAL estradiol)
- Serum TOTAL testosterone LC/MS/MS
(free testosterone is unreliable [33])
- CMP (to include BMP & albumin)

Goals:

Titrate GAT dosing to the physiologic range of non-transgender individual of identified gender (levels vary by lab – Quest lab ranges listed)

- Physiologic range of mid-cycle non-transgender female
 - Estradiol = 64-357 pg/mL (test code 4021 – can google to order)
 - Total Testosterone = 2-45 ng/dL (test code 15983)

No evidence to support extra monitoring: lipids, A1c/glucose, cholesterol

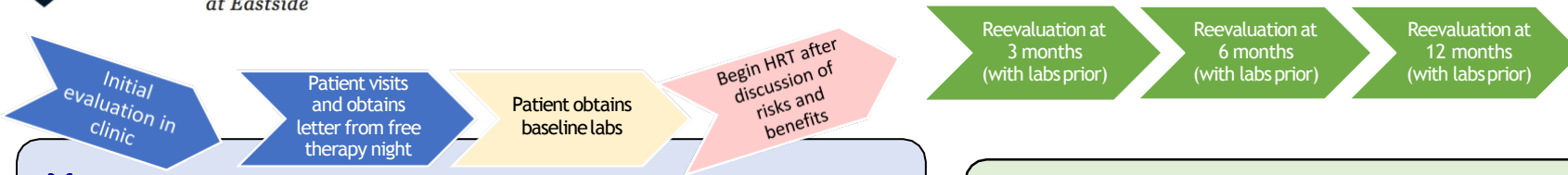
Other Health Concerns

Prostate Exams: follow current guidelines, prostatic atrophy may be severe if on finasteride

Hernias: If pre-operative SRS – MUST monitor – tucking genitals can cause hernias or perineal skin breakdown

If post-operative SRS and needs vaginal exam – NO cervix or fornices – pap smears unnecessary (/impossible)

Visualization of tissue may be better with an anoscope (if necessary, EAC would need WeCare referral)



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 - Desire for fertility – counsel on fertility options
- Set **expectations** for what changes to expect from GAT (reference)
 - Skin oiliness; 1-6 months; 1-2 years
 - Facial/body hair growth; 3-6 months; 3-5 years
 - Scalp hair loss; >12 months; variable
 - Increased muscle mass/strength; 6-12 months; 2-5 years
 - Body fat redistribution; 3-6 months; 2-5 years
 - Cessation of menses; 2-6 months; n/a
 - Clitoral enlargement; 3-6 months; 1-2 years
 - Vaginal atrophy; 3-6 months; 1-2 years
 - Deepened voice 3-12 months; 1-2 years
- Absolute Contraindications: any active estrogen-sensitive cancer
- Complete Informed Consent Form & Upload to patient chart
- Enroll patient in Gender Affirming Therapy in the Clinic Navigator



Therapeutic Options

- Testosterone Cypionate IM or SQ:
- Initial 50 mg/wk; Max 100 mg/wk
 - Can double each dose for q 2-week dosing
- Others (for reference)
- Testosterone Enanthate IM or SQ: Initial 50 mg/wk; Max 100 mg/wk
 - Testosterone topical gel 1%: Initial 50 mg qAM; Max 100 mg qAM
 - Testosterone topical gel 1.62%: 40.5-60.75mg qAM; Max 103.25mg qAM
 - Testosterone Patch: Initial 4 mg qPM; Max 8 mg qPM
 - Testosterone cream: initial 50 mg, Max 100 mg
 - Testosterone Axillary gel 2%: Initial 60 mg qAM; Max 90-120 mg qAM
 - Testosterone Udecanoate: Initial 750 IM repeat in 4 weeks, q 10 weeks

Testosterone Treatment Risks

Erythrocytosis/polycythemia

- Use reference male range
- Management of polycythemia
 - 1) Check testosterone levels, including peak levels – adjust dose
 - 2) More frequent injection schedule with lower peak dose may lower risk [59]
 - 3) Phlebotomy or blood donation short term solution
 - 4) Rule out pathologic causes of polycythemia (OSA, tobacco, etc)

Hair Loss

- Fronto-temporal pattern, severity based on genetics
- *Management*
 - OTC Minoxidil (Rogaine)
 - 5-alpha reductase inhibitors (finasteride/dutasteride)
 - Surgical approaches – scalp advancement, hair transplantation

Acne

- Peaks in first year of testosterone therapy then declines
- Treat as normal with topical skin treatments escalating with severity

Weight gain

- Must use with caution and informed consent with PCOS, obese, or hyperlipidemic patients



Labs Baseline & Prior to Every Visit

- CBC without diff (Hg and Hct for erythropoietic effect)
- Serum Estradiol (not total estradiol)
- Serum Total Testosterone LC/MS/MS (free testosterone unreliable [33])
- Serum Albumin
- No evidence to support extra monitoring: lipids, A1c/glucose, cholesterol

Goals

- Titrate GAT dosing to the physiologic range of non-transgender individual of identified gender (levels vary by lab – Quest lab ranges listed)
- Physiologic range of non-transgender males ≥ 18 yo
 - Total Testosterone = 250-1100 ng/dL (test code 15983)
 - Serum Estradiol = can vary greatly – not great priority
 - Only 29% of 31 trans men achieved physiologic male-range estradiol levels

Health Maintenance

- Pap smears:** follow USPSTF, likely behind, based on age
- Can be traumatizing – “checkitoutguys.ca” is good patient resources for FTM’s
 - MUCH higher rate of inadequate cytologic sampling (possibly due to rushing procedure from patient discomfort)[31]
 - Can pre-medicate with vaginal estrogens 1-2 weeks prior to exam to decrease vaginal atrophy due to testosterone therapy
 - If still refuses – offer external OR bimanual as initial step towards establishing trust