MTF Clinical Approach and Protocols

Gender Health Center, Hormone Clinic
Sacramento, CA
Katherine Gardner, MD
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Name and Pronouns:

Preferred names and pronouns are used at all times when referring to the patient, both when the patient is present and when discussing patients outside the presence of the patient. Because preferred names and pronouns can change, it is important that if, at anytime, the preferred name and pronoun are not known, that the patient is asked. For rare instances when the preferred name and pronoun cannot be used (for example, on prescriptions when the current legal name must be used), the patient is notified that this is happening and why it is happening.

Informed Consent Model of Prescribing:

Hormones are prescribed based on a informed consent model. The informed consent model requires: 1) thorough medical, surgical, social, psychiatric, and gender history 2) that the provider has an understanding of what the patient wants from hormones, allowing appropriate counseling regarding expectations 3) extensive counseling regarding the effects of estrogen, long-term, short-term, permanent 4) discussion of risks of estrogen 5) discussion regarding impact on fertility 6) no medical contraindications 7) capacity to provide medical consent or the consent of those who make medical decisions for the patient. Counseling and therapy is NOT required however, as it is for any patient, if appropriate, based on mood symptoms identified during the appointment, it is strongly recommended.

General Guiding Principles of Prescribing Hormones for Medical Transition:

The goal of therapy is to achieve effects identified by the patient as important to them. Because of this, the focus of all appointments is talking with the patient about their expectations/concerns and counseling about the expected effects and timelines.

Antiandrogens and estrogens should be prescribed together. The reason if this is that with adequate suppression of endogenous androgens, less estrogen is needed to achieve feminizing effects.

Because the goal of therapy is to achieve effects desired by the patient, medications should be titrated to effect within protocol parameters rather than according to lab values. However, if there is concern about dosing or question about appropriate titration, can consider:

1) Serum testosterone should be in female range (<55 ng/dl).
2) Serum estradiol should be in mean daily range for premenopausal women (<200 pg/mL) HOWEVER conjugated estrogens which is what we prescribe when prescribing oral estradiol cannot be measured in the serum so this test is not useful for our patients taking oral estradiol. *Endocrine Treatment of Transsexual Persons: an Endocrine*

Gender Health Center, Hormone Clinic
2020 29th St #201 Sacramento, CA 95817

Society Clinical Practice Guideline, September 2009

Medications:

Antiandrogens:

1) Spironolactone: most commonly used and strongest known antiandrogen. Works by directly inhibiting testosterone secretion and by inhibiting androgen binding to androgen receptors. There is some speculation that it may also have estrogenic activity.

- Dosed once daily
- Comes in 25, 50, 100mg tabs (25mg tabs are the only size currently covered by MediCal)
- Patients who have had an orchiectomy will often stop spironolactone or continue on at a very low dose

2) Finasteride: type II alpha 5 reductase inhibitor. Competitively binds to alpha 5 reductase, the enzyme that converts testosterone to dihydrotestosterone (more potent androgen than testosterone).

- Not commonly used because spironolactone is known to have a much stronger antiandrogen effect and has fewer side effects. Finasteride is known to increase depression and anxiety, both of which are common in our patient population. There is no evidence to suggest that adding finasteride to spironolactone rather than just increasing spironolactone has a better antiantrogenic effect.
- For patients who are unable to tolerate spironolactone or who we are unable to achieve adequate suppression of testosterone with spironolactone alone (uncommon) finasteride can be prescribed either alone or in conjunction with spironolactone

Hormones:

1) Estradiol: oral tablets. Use minimal effective dose. High dosing can be used for several years at the initiation of therapy then decreased after maximal breast growth and other desired changes are achieved. In our clinic, oral estradiol is only prescribed to patients under the age of 40 because it has a slightly higher risk of thrombosis than other forms of estradiol.

- Some patients have heard that using the tabs sublingual is better. I think this is because in theory, it would bypass the liver so they get higher doses. I advise against this because the dose they can get will be variable with SL use and if they find that the oral dosing is not giving satisfactory results, estradiol or spironolactone can be titrated up
- Dosed once daily
- Comes in 1mg and 2 mg tabs, both covered by most insurance in California

2) Estrogen Patches: Safer way to deliver estrogen (compared to oral estradiol) to people who are at higher risk for the CV, stroke, or thrombotic effects of estrogen because it bypasses first pass metabolism in the liver. Estradiol patches and injectable estradiol are the preferred method of delivery for patients over 40.

- Comes in 0.05mg/24 hr and 0.1mg/24 hr patches

- Dosed once every 5 days
- Covered by most insurance in California (including MediCal)

3) Estradiol Valerate: Another safer way to deliver estrogen (compared to oral estradiol) to people who are at higher risk for the thrombotic, CV, and stroke effects of estrogen because it bypasses first pass metabolism in the liver. Estradiol patches and injectable estradiol are the preferred method of delivery for patients over 40. The patient needs to be taught how to safely self inject into the quadricep muscle.

- Comes in 10mg/mL and 20mg/mL
- Dosed every 14 days
- Covered by most insurance in California (including MediCal)

4) Estrogen Creams: Many different forms and concentrations. Avoids first pass metabolism in liver however dosing and absorption is much more variable. Therefore the effect is less stable and predictable. Dosing is less clear. Not commonly used. Not prescribed in our clinic

5) Progesterone: In women with uterus, main effect is on uterine lining and is not thought to have significant effect on breast growth or feminization (based on limited studies in MTF patients). Additionally, progesterone has significant side effects (HA, nausea, acne, etc) Because of this, we don't use it.

Other Considerations:

- For patients who have had an orchiectomy, spironolactone or other antiandrogens are either stopped or significant decreased. Additionally, estradiol dose is also often decreased after orchiectomy if the patient has been on high dose.
- Cost:
    - Spironolactone, oral estradiol, patches, and injectable estradiol is covered by the majority of insurance companies in California
        - To fill out prior authorization or TAR, diagnosis is Endocrine Disorder NOS ICD-9 code: 259.9; Medical Necessity: Estradiol and spironolactone are the two most commonly used medications for treatment of FTM gender identity disorder.
    - For cash paying patients, least expensive place to get spironolactone and estradiol is Costco, Target/Walmart

Prescribing Protocols:

MTF Standard Protocol:

Criteria:

- Age >18, <40
- Able to provide consent
- Exclusion from standard protocol: current smokers or ex-smokers who have quit <3 months ago, blood pressure >140/90
- Absolute contraindications: history of thromboembolic disease, macroprolactinoma, breast cancer, severe liver dysfunction (transaminases >3x upper limit of normal), coronary artery disease, cerebrovascular disease, severe migraines (ocular migraines), active cocaine or methamphetamine use (need to be clean x 3 months)

Rx	Initial	Standard	High
Estradiol (1mg or 2mg tabs)	2mg PO daily 1 tab PO daily	4mg PO daily 2 tabs PO daily	6mg PO daily 3 tabs PO daily
Spironolactone (25mg tabs)**	100mg PO daily** 4 tabs PO daily**	200mg PO daily** 8 tabs PO daily**	300mg PO daily**

* Assess smoking status and blood pressure at each visit

** Can be broken up into BID dosing if needed

MTF Low Dose Protocol (used for active smoker)

Criteria:

- Age >18, <40
- Able to provide consent
- Absolute contraindications: history of thromboembolic disease, macroprolactinoma, breast cancer, severe liver dysfunction (transaminases >3x upper limit of normal), coronary artery disease, cerebrovascular disease, severe migraines (ocular migraines), active cocaine or methamphetamine use (need to be clean x 3 months)

Rx	Initial-Standard	
Estradiol (1mg tab)	1mg PO daily 1 tab PO daily	Can move to standard protocol once BP controlled or smoking cessation x 3mo
Spironolactone (25mg tabs)**	Use standard protocol dosing	

* Assess smoking status and blood pressure at each visit

** Can be broken up into BID dosing if needed

MTF Protocol (Age >40, or at elevated risk for thrombotic, CV disease)

Criteria:

- Age >40 or at elevated risk for thrombotic or cardiovascular disease
- Able to provide consent
- Nonsmoker, normotensive, no cocaine/methamphetamine use within the last 3 months
- Absolute contraindications: history of thromboembolic disease, macroprolactinoma, breast cancer, severe liver dysfunction (transaminases >3x upper limit of normal), coronary artery disease, cerebrovascular disease, severe migraines (ocular migraines), active cocaine or methamphetamine use (need to be clean x 3 months)

Patch Estradiol Dosing

Rx	Initial	Standard	High
Estradiol Patch	Estradiol 0.1mg/24 hour patch q 5 days	Estradiol 0.1mg/24hr patch q 5 days	2 estradiol 0.1mg/24hr patches q 5 days
Spironolactone**	100mg PO daily**	200mg PO daily**	300mg PO daily**

Assess smoking status and blood pressure at each visit
Titration q3 months
** Can be broken up into BID dosing if needed

Intramuscular Estradiol Valerate Dosing

Rx	Initial/Low Dose	Standard	High
Estradiol Valerate 10mg/mL OR 20mg/mL concentration	10mg q 14 days 1cc q 14 days	20mg q14 days 0.75-1 cc q14 days	Same as standard dose
Syringe	1cc syringe #15	1cc syringe #15	
18 gauge 1.5 inch needle to be used for drawing	#15	#15	
22 gauge 1 inch needle to be used for injecting	#15	#15	
Spironolactone**	100mg PO daily**	200mg PO daily**	300mg PO daily**

Assess smoking status and blood pressure at each visit
Titration q3 months
** Can be broken up into BID dosing if needed

MTF Protocol (16-17 yo)
Criteria

- Age 16-17
- Able to understand discussed effects/permanent changes/risks, guardian consent also required
- Connected to regular counseling, peer group meetings etc strongly recommended
- No tobacco, cocaine, methamphetamine use

General concept is to start lower and work up slower than with >18 yo

Rx	Initial	Standard	High
Estradiol (1mg or 2mg tabs)	1mg PO daily 1 tab PO daily	4mg PO daily 2 tabs PO daily	6mg PO daily 3 tabs PO daily
Spironolactone (25mg tabs)**	50mg PO daily** 2 tabs PO daily**	200mg PO daily** 8 tabs PO daily**	300mg PO daily**

* Assess smoking status and blood pressure at each visit
** Can be broken up into BID dosing if needed

MTF Protocol (<16 yo)
Based on
1) UCSF Center of Excellence for Transgender Health
http://transhealth.ucsf.edu/trans?page=protocol-youth
2) Expert opinion through Transgender Medical Consultation Service
3) *Endocrine Treatment of Transsexual Persons: an Endocrine Society Clinical Practice Guideline*, September 2009
Criteria:
- Tanner Stage II or greater
- Participation in counseling. Can be individual, group or family

Currently, our clinic is not prescribing hormones to patients under the age of 16. This is not because patients under 16 cannot be prescribed hormones but because the structure of our clinic does not provide an environment in which it is responsible to prescribe to patients under 16. Patients under 16 will require multiple frequent visits with their families and likely more extensive counseling/exploration of when it would be an appropriate time to start hormones leading up to the decision to initiate hormone therapy. Currently, our clinic operates 2 Friday nights a month without a way for families or patients to contact us outside of these clinic hours. As our clinic changes, our hope is to be able to accommodate younger patients. Patients under age 16, can and are safely prescribed hormones by providers in other settings (for example a clinic that has weekday hours and who has medical coverage throughout the week).

“Puberty Blockers:”
Idea is that after reaching Tanner Stage II (which can happen between ages (8-12), puberty should be held off until the patient is mature enough to fully understand the effects/permanent changes/risks of testosterone. The reasoning behind this thought is not backed by the data that

currently exists on trans youth. From all data, it seems that once a child enters puberty, gender identity is consistent with their future gender identity of adulthood. Studies have found that all adolescents who identify with a gender other than their assigned gender at birth have this identity persist into adulthood. This is not the case for children prior to puberty who identify as a gender other than their assigned gender at birth.

GnRH, leuprolide 7.5mg IM monthly, comes in 7.5mg vials
Depo Provera q 12 weeks

Considerations:
1) Cost: GnRH is very expensive, several hundred dollars for a vial which is only a month - HOWEVER recently, this has been covered by most California insurance companies
2) Effect, while patients won't experience feminizing effects with leuprolide, benefit is that hair growth on the face and body will stop increasing, voice will stop deepening, muscle build up will stop

Lab Protocol:

Initial Visit:	Every 3 months until on a stable dose	Every 6 months once on a stable dose	3 months after any dose change
CBC, CMP, prolactin (if previously on hormones)	CBC, CMP, prolactin	CBC, CMP, prolactin	CBC, CMP, prolactin

Follow Up Protocol:
Every 3 months until on a stable dose, every 6 months once on a stable dose. Make sure to bring in the patient for follow up 3 months after any dose change.

Health Maintenance and Screening Protocol:

- Appropriate screening for prostate cancer. No clear guidelines currently on how to screen for prostate cancer. Important to remember for women with a neovagina, can palpate the prostate through the vagina rather than with a digital rectal exam.
- Breast Cancer Screening: Mammography based on current screening guidelines
- STI screening as appropriate (assess with every visit)
- Assess if candidate for PrEP
- Colon cancer screening starting at age 50
- Assess blood pressure at every visit (at increased risk for HTN due to estrogen use)

Expectations:

From Endocrine Treatment of Transsexual Persons: an Endocrine Society Clinical Practice Guideline, September 2009

Based on dosing at standard level

Effect	Starts (months)	Maximum effect (years)
Breast Growth	3-6 months	2-3 years
Softening of skin/decrease in oiliness of skin	3-6 months	Unknown
Scalp hair	Does not regrow	Does not regrow
Voice changes	No change	No change
Decreased hair growth on face, arms, legs	6-12 months	Over 3 years
Decrease in sex drive	1-3 months	3-6 months
Decrease in morning/spontaneous erections	1-3 months	3-6 months
Difficulty obtaining an erection	Varies between individuals	Varies between individuals
Decrease in muscle mass	3-6 months	1-2 years
Change in distribution of body fat	3-6 months	2-3 years
Decrease in sperm count	unknown	Over 3 years
Decrease in testicular volume	3-6 months	2-3 years

REFERENCES:

1) World Professional Association for Transgender Health. Standards of Care (SOC) for the Health of Transsexual, Transgender, and Gender Nonconforming People, 7th version: http://www.wpath.org/publications_standards.cfm

2) Center of Excellence for Transgender Health, UCSF. Primary Care Protocol for Transgender Patient Care: http://transhealth.ucsf.edu/trans?page=protocol-00-00

3) Clinical Protocol Guidelines for Transgender Care. Vancouver Coastal Health: http://transhealth.vch.ca/resources/careguidelines.html

4) Endocrine Society's Clinical Guidelines: *Endocrine Treatment of Transsexual Persons: an Endocrine Society Clinical Practice Guideline, September 2009* www.endosociety.org/guidelines/final/upload/endocrine-treatment-oftranssexual-persons.pdf

5) UCSF Center of Excellence for Transgender Health http://transhealth.ucsf.edu/trans?page=protocol-youth

6) Lyon-Martin Clinical Guidelines http://lyon-martin.org/services/transgender/

7) Gender Health Center, Sacramento (916) 455-2391 http://www.thegenderhealthcenter.org/

8) Trans Line http://project-health.org/transline/

9) Transgender Law and Policy Institute http://transgenderlaw.org/

With any questions:

Katherine Gardner, MD
Gender Health Center, Hormone Clinic Medical Director
Email: katherinegardner@gmail.com
Cell: 858-232-8107

Gender Health Center
2020 29th St #201 Sacramento, CA 95817
(916) 455-2391