GENDER-AFFIRMING HORMONE THERAPY

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GOALS AND OBJECTIVES

1. Review process of initiating hormone therapy through the informed consent model

2. Provide an overview of masculinizing and feminizing hormone therapy

3. Review realistic expectations and benefits of hormone therapy vs their associated risks

4. Discuss recommendations for monitoring
PROTOCOLS AND STANDARDS OF CARE
The criteria for hormone therapy are as follows:

1. Well-documented, persistent (at least 6 mo) gender dysphoria
2. Capacity to make a fully informed decision and to consent for treatment
3. Age of majority in a given country
4. If significant medical or mental health concerns are present, they must be reasonably well controlled
INFORMED CONSENT MODEL

- Requires healthcare provider to
  - Effectively communicate benefits, risks and alternatives of treatment to patient
  - Assess that the patient is able to understand and consent to the treatment

- Informed consent model does not preclude mental health care!
- Recognizes that prescribing decision ultimately rests with clinical judgment of provider working together with the patient

- Recognizes patient autonomy and empowers self-agency
- Decreases barriers to medically necessary care
INITIAL VISITS

- Review history of gender experience
- Document prior hormone use
- Review patient goals
- Assess appropriateness for gender affirming medical treatment
  - Address safety concerns
  - Assess social support system
- Obtain informed consent
  - Review risks and benefits of hormone therapy
- Assess medical safety
  - CPE
  - Obtain sexual history
  - Order screening laboratory studies
- Provide referrals
GENDER NARRATIVES

A gender narrative refers to a personal history of experienced gender awareness, development, exploration, acceptance/rejection, identification, persistence, and clarification

▪ INDIVIDUAL, there is no one, “right” story
  ex: I was born in the wrong body. I only played with girls toys growing up

▪ Things to consider
  ▪ Intersectionality - the complexity of multiple identities overlapping and existing together (gender, race, socioeconomic status, religious beliefs, age, ability, etc)
  ▪ Non-binary/Queer/GD
  ▪ Gender narratives and identities are fluid
TAKING A HISTORY

- Same as for all patients, but pay specific attention to health disparities
- Be aware of contexts that increase health risks
  - What are risk factors for smoking, substance use, or engaging in sexual risk behaviors? What is the incidence of trauma/abuse in this population?
- Ask about social support; be aware of possible rejection by family or community of origin, harassment, and discrimination
- Ask about previous use of hormones, gender affirmation surgeries, and use of silicone
MEDICAL DECISION MAKING

Remember ...

4. If significant medical or mental health concerns are present, they must be *reasonably well controlled*

- Take your time
  - What is reasonable in terms of control?
  - Consider the role of harm reduction
  - Refer to specialist if needed (remember, YOU are the gender specialist! and may need to educate and also advocate for your patient)
  - Try not to let your timeline and anxiety get intertwined with your patients’ timeline and pressures
    - Work together. Be transparent. ...
LABORATORY MONITORING
BASELINE

Transmasculine
- CBC (Hgb/Hct)
- Lipid Profile, only as clinically indicated
- Liver Enzymes, only if evidence of underlying liver disease
- Fasting Glucose, only if clinically indicated
- Screen for PCOS with +ROS, ??

Transfeminine
- Baseline kidney function
- Lipid Profile, only as clinically indicated
- Liver Enzymes, only if evidence of underlying liver disease
- Fasting Glucose, only if clinically indicated
GENDER-AFFIRMING HORMONE THERAPY
MASCU LINIZING HORMONE OPTIONS

Injectable Testosterone

- Testosterone Enanthate or Cypionate IM or SC, q1 or 2 weeks

- Weekly Dosing versus Biweekly Dosing
  - Consider susceptibility of peak/trough levels with biweekly dosing. Consider mental health diagnosis

- **Standard Weekly Dose**: 50 – 100 mg / week
  - Starting at 50mg/week and increase in 1 month

- **Standard Biweekly Dose**: 150-200 mg / 2 weeks
  - Starting with 100mg/biweekly and increase in 1 month
TRANSDERMAL TESTOSTERONE

• Patches
  ▪ Androderm: (2 & 4mg patches) Apply 2-8mg/day

• Topical gels in packets and pumps
  • Apply 50 – 100mg/day
    ▪ Androgel pump: 1.62% gives 20.25mg per pump
      • 2 pumps for starting dose
    ▪ Androgel or Testim packets: 25mg (2.5gm) or 50mg (5gm)
      • Generally start with 50mg packet
      • Intended to be applied to Arm > Abdomen > Inner thigh
    ▪ Axiron 2% pump gel for axillary application: 1 pump (30mg) to each axilla daily
OTHER OPTIONS

Testosterone Pellet
- Testopel - Implant 8-12 pellets q 3 to 4 months

Testosterone undecanoate
- AVEED - Injectable long-acting. 750mg/3mL injection every 10wks, with initial loading dose
ADDITIONAL MEDICATIONS

- **Testosterone cream/DHT cream** for clitoral enlargement
- **Estrogen vaginal cream** for atrophy
  - Also can be used for inadequate pap tests
- **Rogaine or Finasteride** for male pattern baldness
- **Progesterone** – LARC (IUD, Nexplanon), Depo, which may aid in cessation of menses before or after starting testosterone therapy
## TIMELINE FOR MASCULINIZING EFFECTS

<table>
<thead>
<tr>
<th>Effect</th>
<th>Onset (months)</th>
<th>Maximum (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin oiliness/acne</td>
<td>1-6</td>
<td>1-2</td>
</tr>
<tr>
<td>Fat redistribution</td>
<td>1-6</td>
<td>2-5</td>
</tr>
<tr>
<td>Cessation of Menses</td>
<td>2-6</td>
<td></td>
</tr>
<tr>
<td>Clitoral enlargement*</td>
<td>3-6</td>
<td>1-2</td>
</tr>
<tr>
<td>Vaginal atrophy</td>
<td>3-6</td>
<td>1-2</td>
</tr>
<tr>
<td>Emotional changes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased sex drive</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table: Menopausal Symptoms and Onset/Maximum Duration

<table>
<thead>
<tr>
<th>Effect</th>
<th>Onset (months)</th>
<th>Maximum (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deepening of voice*</td>
<td>3-12</td>
<td>1-2</td>
</tr>
<tr>
<td>Facial/Body Hair Growth*</td>
<td>6-12</td>
<td>4-5</td>
</tr>
<tr>
<td>Scalp Hair Loss*</td>
<td>6-12</td>
<td></td>
</tr>
<tr>
<td>Increased Muscle Mass &amp; Strength</td>
<td>6-12</td>
<td>2-5</td>
</tr>
<tr>
<td>Coarser Skin/ Increased Sweating</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight Gain/Fluid Retention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild Breast Atrophy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weakening of Tendons</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: * indicates symptoms that are commonly associated with menopause.
RISKS OF TESTOSTERONE THERAPY

- Lower HDL & Elevate TG
- Polycythemia/erythrocytosis
  - Limited long-term data: breast, endometrial tissue, ovarian tissue
    - Good short-medium term data!
- Increased risk of sleep apnea
- Increase insulin resistance?
- Infertility
- Pelvic pain
- Mental health effects
- Hepatotoxicity (with oral formulations)
  - Much less risk with parenteral formulations
FOLLOW UP LAB MONITORING

Serum testosterone levels
- At 6 and 12 months, then as clinically indicated
- If using topical, consider checking testosterone level at 3 months
- May be checked 6 to 12 weeks after dosage change
- Goal Range: ~350-900 ng/dl

Estradiol levels?
Goal Range: less than 50 pg/ml
- Do not need to check if T in therapeutic range.
- Only check if not masculinizing, abnormal bleeding, etc.
FOLLOW UP LAB MONITORING

After 6 months → then every 6 to 12 months

- Hct/Hgb
- Lipid Profile, as clinically indicated
- Fasting Glucose or HbA1c, as clinically indicated
  - Testosterone may impact glucose metabolism, increasing insulin resistance
FEMINIZING HORMONE OPTIONS

Oral Estrogens
- Estradiol (estrace) 2-8 mg PO or SL daily (can be divided into BID dosing)
- Premarin (conjugated estrogens) 1.25-10mg PO daily (can be divided into BID dosing)

Injectable Estrogens
- Estradiol valerate 5-20mg IM q2 weeks
- Estradiol cypionate 2-10mg IM weekly

Transdermal Estrogens
- Estradiol patch 0.1-0.4mg twice weekly, may start lower in patients at risk of side effects. Maximum single dose patch available is 0.1 mg
ANTIANDROGENS

- **Spironolactone** (aldactone) 50-400mg PO daily (can be divided into BID dosing)

- 5-alpha reductase inhibitors: finasteride (Proscar) and dutasteride - Inhibits conversion of testosterone to DHT

- Casodex (bicalutamide) - non-steroidal androgen receptor inhibitor

- Lupron $$$ - Leutinizing hormone (LH) releasing hormone agonist, more simply called a GnRH agonist

- Cyproterone acetate - synthetic progestagen with strong anti-androgen activity
WHAT ABOUT PROGESTINS?

- Benefit on breast development
- Part of the “natural” female hormonal make-up

Risks
- Associated with increased risk of cardiovascular events and breast cancer in WHI - but how does this translate to trans women?
- Also risk of weight gain and depression
- No clear evidence of affect on breast growth!

Benefits
- Weight gain!, moodiness!/cycling
- Improved mood
- Improved libido, energy
BREAST DEVELOPMENT IN TRANS WOMEN

Clinical review: Breast development in trans women receiving cross-sex hormones.

Wierckx K¹, Gooren L, T'Sjoen G.

11 studies, just under 1000 patients

Only 3 studies with more than 100 subjects

Generally poor quality studies. How to objectively measure the breast? Many used subjective measures of breast satisfaction or wish for breast augmentation

CONCLUSIONS:

Our knowledge concerning the natural history and effects of different cross-sex hormone therapies on breast development in trans women is extremely sparse and based on low quality of evidence. **Current evidence does not provide evidence that progestogens enhance breast development in trans women.** Neither do they prove the absence of such an effect. This prevents us from drawing any firm conclusion at this moment and demonstrates the need for further research to clarify these important clinical questions.
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PROGESTINS

- Prometrium 100 mg – 200 mg po daily*
- Provera 2.5 to 10 mg PO daily
- Depo-Provera 150 mg IM q 3 months

Consider daily, even dosing vs cyclic administration of oral progestin: 10 days each month, to lower total exposure to progestin and/or to more closely mimic female physiology.

![Progesterone](image)
# Feminizing Effects of Estrogens & Antiandrogens

<table>
<thead>
<tr>
<th>Effect</th>
<th>Onset (months)</th>
<th>Maximum (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased Libido</td>
<td>1-3</td>
<td>3-6</td>
</tr>
<tr>
<td>Decreased Spontaneous Erections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast Growth*</td>
<td>3-6</td>
<td>24-36</td>
</tr>
<tr>
<td>Decreased Testicular Volume*</td>
<td>3-6</td>
<td>24-36</td>
</tr>
<tr>
<td>Decreased Sperm Production*</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Redistribution of Body Fat</td>
<td>3-6</td>
<td>24-36</td>
</tr>
<tr>
<td>Decrease in Muscle Mass</td>
<td>3-6</td>
<td>12-24</td>
</tr>
<tr>
<td>Softening of Skin</td>
<td>3-6</td>
<td>Unknown</td>
</tr>
<tr>
<td>Decreased Terminal Hair</td>
<td>6-12</td>
<td>&gt;36</td>
</tr>
</tbody>
</table>

**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
- Mental health effects
- Infertility
RISKS OF SPIRONOLACTONE THERAPY

- Increased urinary frequency
- Hyperkalemia
  - Co-administration with ACE inhibitor or ARB
- Hypotension
- Dehydration and renal insufficiency
  - Co-administration with HCTZ
LAB MONITORING FOR TRANS FEMININE PATIENTS

▪ Serum testosterone level (at 6 to 12 months)
  ▪ Should be less than 55 ng/dl

▪ Serum Estradiol Levels (?)
  ▪ Ideal level is the mean daily level for premenopausal women (about 100 to 200 pg/ml)
  ▪ Timing of blood draw?
LAB MONITORING FOR TRANS FEMININE PATIENTS

- If on spironolactone —
  - BUN/Cr and serum electrolytes 2 to 6 weeks after start/dosage change
  - every 3 months in first year
  - then yearly

- Lipids, glucose, LFTs only as clinically indicated
  - Prolactin level ?? vs only with +ROS

- Hgb/Hct will often drop into the normal female range in women on GAHT
FOLLOW UP CARE FOR GENDER-AFFIRMING HORMONE THERAPY

- Assess masculinization or feminization
  - Think about particular considerations for non-binary, gender fluid, and gender queer patients
    - Low dose hormones, surgery w/o hormones, short term hormone use, etc
- Review medication use
- Monitor mood cycles and adjust medication as indicated
- Discuss social impact of transition
- Counsel regarding sexual activity
  - Remember that this can change! Sexual orientation, experimentation, increased confidence, increased libido
- Review surgical options
- Plans change of name and gender marker on legal forms
- Review CAD risk factors
- ASSESS SAFETY
NON-BINARY INDIVIDUALS

- Adjust doses of spironolactone and/or estradiol to maintain testosterone levels in a range between standard male and female levels
- Use of anti-androgens alone
- Limited courses of hormone therapy
- Surgical affirmation without hormone treatment
HORMONE THERAPY AND AGING

- Many gender diverse individuals start gender-affirming therapy at later ages; may experience slower and less vigorous changes
- Co-occurring medical issues may increase risk
- No clinical evidence to guide us on how long to continue hormone therapy
- Consider lowering dose of estrogen or testosterone around age 50, if patient has been on therapy for a number of years. Likely little benefit in stopping — maybe 65??
Questions?