TESTOSTERONE THERAPY

Helena Turner, MSN, FNP-C, AAHIVS
Fenway Health
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EDUCATION CENTER
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GOALS AND OBJECTIVES

1. Review pre-prescription counseling and understanding patient goals for care

2. Provide an overview of testosterone therapy options and considerations when choosing

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

4. Discuss recommendations for monitoring

PROTOCOLS AND STANDARDS OF CARE

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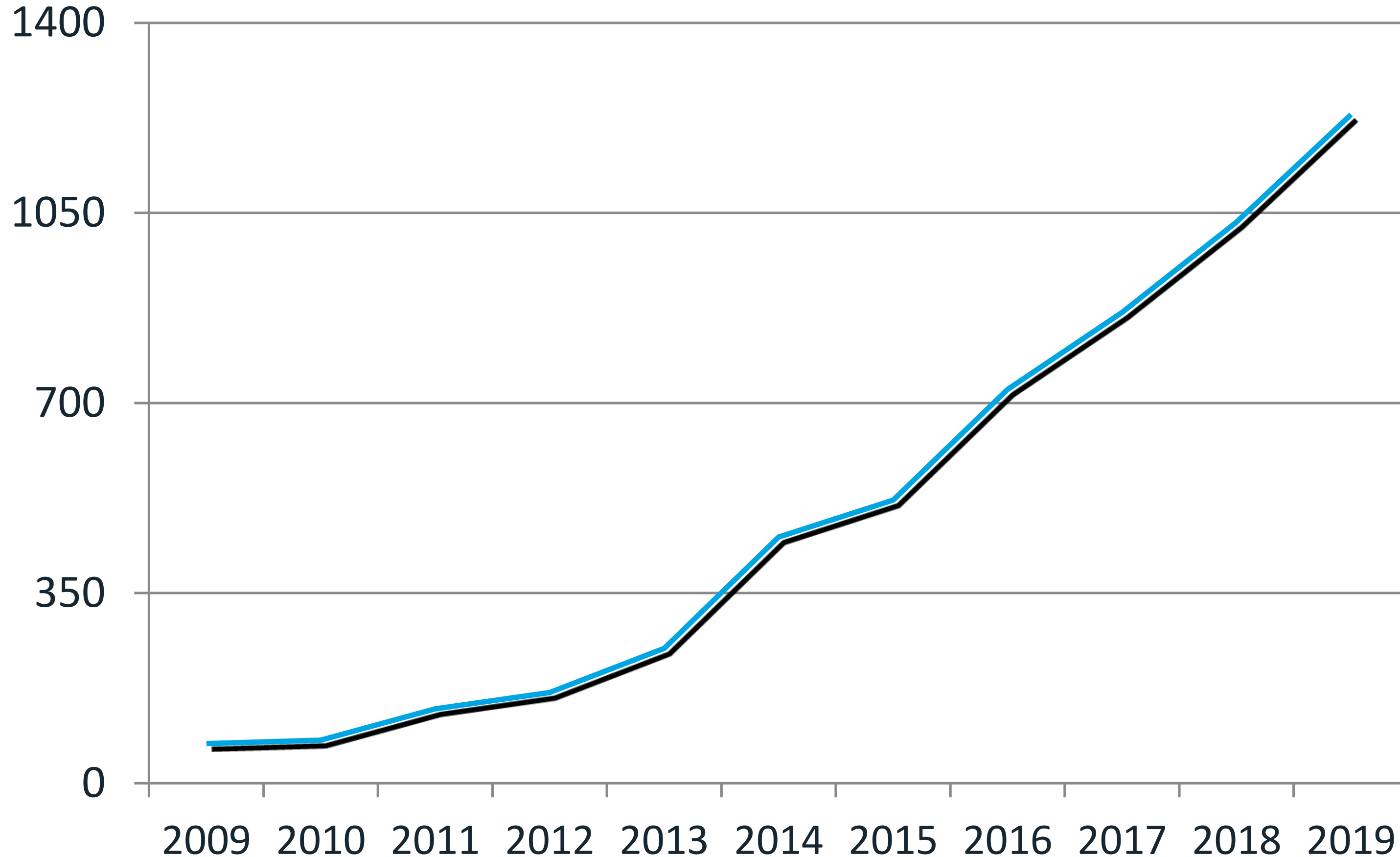
- Primary Care Protocol for Transge

10 YEARS OF TRANSGENDER HEALTH RESEARCH:
Number of Peer-Review Publications, 2009-2019



Search performed 10/31/19
Slide courtesy of Dr Sari Reisner

TESTOSTERONE THERAPY

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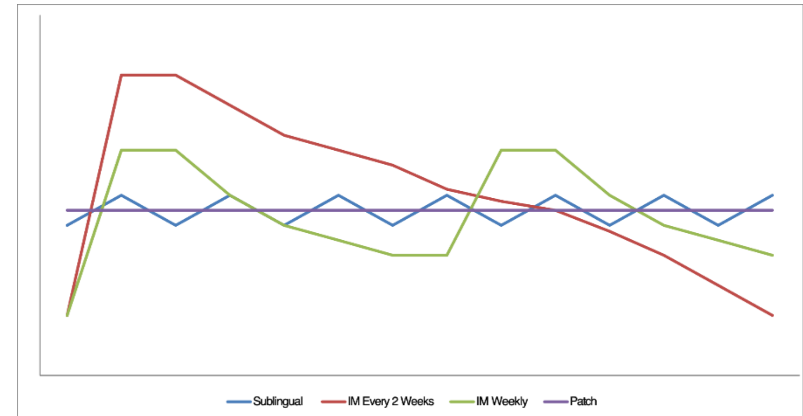
TESTOSTERONE OPTIONS

- **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

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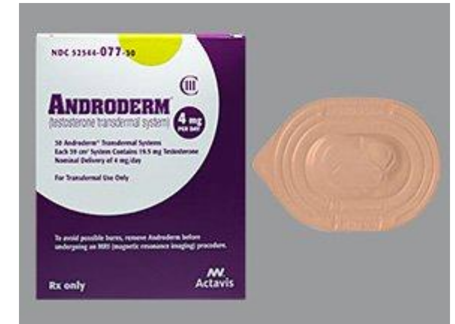
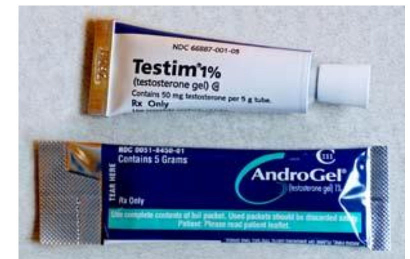
TRANSDERMAL TESTOSTERONE



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

- **Topical gels in packets and pumps**
  - Apply 50 – 100 mg / day

  - Androgel pump: 1.62% gives 20.25 mg per pump
    - 2 pumps for starting dose
  - Androgel or Testim packets: provide 25 mg (2.5 gm) or 50 mg (5 gm)
    - Generally start with 50mg packet
    - Intended to be applied to Arm > Abdomen > Inner thigh
  - Axiron 2% pump gel for axillary application: 1 pump (30 mg) to each axilla daily



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Project ECHO®

ADDITIONAL 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

EFFECTS OF TESTOSTERONE THERAPY

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		

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CONTINUED…

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		
Mild Breast Atrophy		
Tendon Injury		

RISKS OF TESTOSTERONE THERAPY

- Shift in lipid profile: Lower HDL & Elevate TG
- Erythrocytosis
- Limited long-term data: breast, endometrial tissue, ovarian tissue
  - Good short-medium term data! — NO increased risk of cancer
- Increased risk of sleep apnea
- Increase insulin resistance?
- Infertility
- Pelvic pain
- Mental health effects
- Hepatotoxicity (with oral formulations)
  - Much less/no risk with parenteral formulations

LAB MONITORING for TESTOSTERONE THERAPY

- **Baseline labs:**
  - **CBC (Hgb/Hct)**
  - Lipid Profile, Fasting Glucose — based on USPSTF recommendations
  - Screen for PCOS with +ROS — consider closer eval of DM screening?

- **Serum testosterone levels**
  - Goal Range: same as physiologic levels of non-trans men (~350-900 ng/dl)
  - Could consider lower levels for those not interested in as robust or quick changes

- **Estradiol levels?**
  - Goal Range: less than 50 pg/ml
  - Do NOT need to check regularly
  - Only check if abnormal bleeding, administering very low dose T

LAB MONITORING for TESTOSTERONE THERAPY

Labs	Baseline	3mo	6mo	12mo	Yearly	PRN	Additional Comments
Total testosterone		X	X	X	X	X	
Estradiol						X	
Hematocrit	X		X	X	X	X	
Lipids	X					X	only as recommended by current USPSTF guidelines
Glucose or A1c	X					X	only as recommended by current USPSTF guidelines

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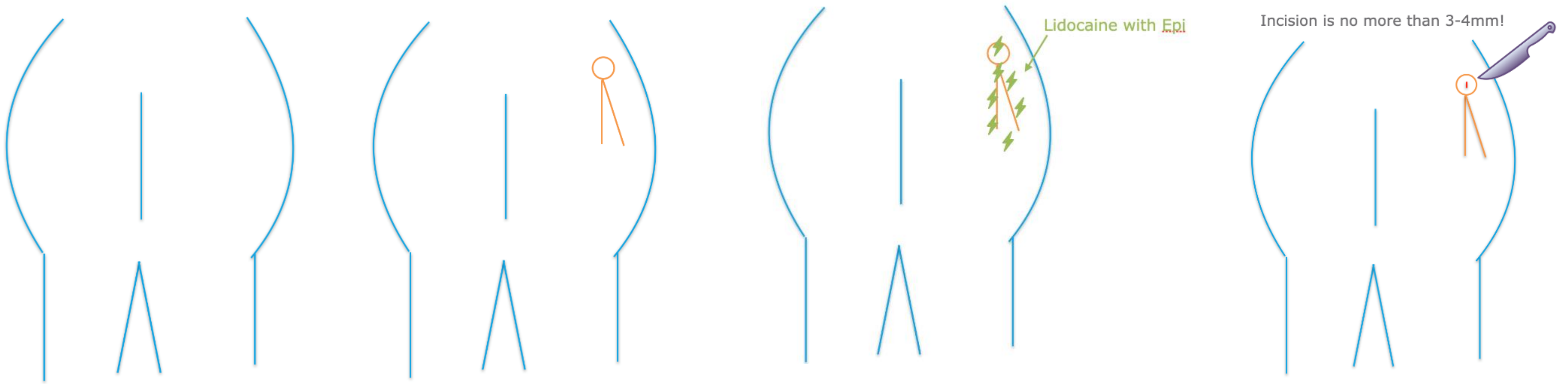
Case of J

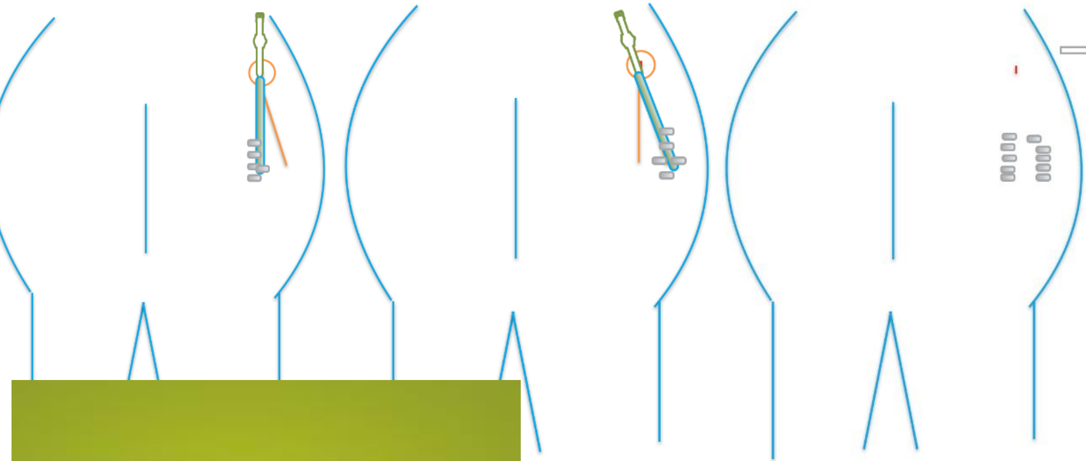
- J is a 24yo AFAB gender queer individual on gender-affirming testosterone therapy for the past 2-3 years. Referred to me for Testopel insertion, as they cannot tolerate self-injection
- Needlephobia leading to missed doses, which then worsens anxiety and dysphoria
- Reports they have been on topical gel in the past, but would experience occasional breakthrough bleeding/spotting due to poor absorption/low levels. Menses causes LOTS of dysphoria
- In talking about the above, they say, "Really the only reason I'm on higher levels of T is to stop the bleeding. Testosterone is important for me, but lower levels would probably be more affirming"

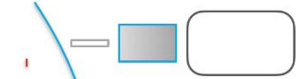
What are their options?

Case of J

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



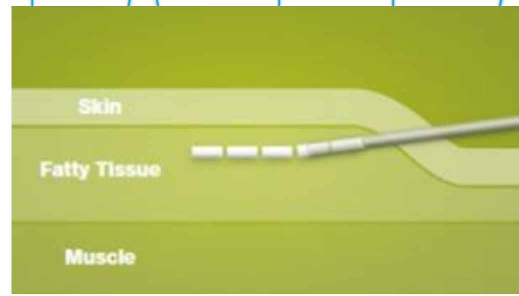




* <u>Instructions</u>:
 - Ice immediately after for 20min
 - Ibuprofen for the next week as needed, but certainly over the 1st few days

 - Avoid swimming or soaking in tub. OK TO SHOWER

* Patients are asked to get total testosterone level checked at <u>1mo</u> and <u>3mo</u> post-insertion after 1st cycle or change in dose



TESTOPEL® 75mg
(testosterone pellets) CIII

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TESTOPEL

- **Expectations**
  - Soreness and bruising
    - Worst 1st time around
    - First few days painful, but then gradual improvement over 1wk
    - NSAIDS and ice!!!
  - Bumps or extrusions
    - Encapsulation of pellets can occur - firm bumps, localized pain w/ palpation/pressure
      - Warm compress, light massage
      - Rare to have to remove
    - Extrusion of a pellet is rare - ~1%. Non-painful pimple or small abscess
      - Nothing much to do with this except sympathize and reassure

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TESTOPEL

- **Complications**
  - Infection
    - Warmth, redness, tenderness, fevers, chills
  - Incision dehiscence
    - It's so small and pellets are far away - pretty minor "complication"
    - Re-bandage with bandaid vs steri strip
  - Persistent pain
    - Make sure using ice and taking NSAIDS
    - Limit exercise/activity for few days after insertion

Considerations

- Person to person inconsistencies
- Insertion to insertion inconsistencies
- It's long-acting so in and effective for at least 3mo

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TRANSDERMAL TESTOSTERONE

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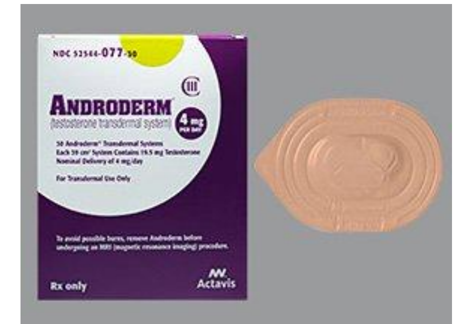

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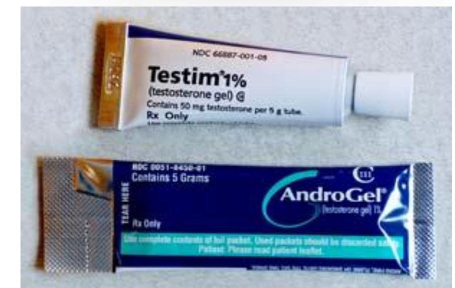

Case of J

- **Low dose testosterone**
  - Gels are great for this! — Low dose, daily vs every other day. Easy to stop and/or adjust.
  - Testopel is long-acting and can lead to high peaks. More unpredictable. Once it's in, it's in!

- **Cessation of menses**
  - Progesterone: LARCs (Nexplanon, IUD), norethindrone acetate
    - Risk of spotting and/or irregular menses with LARCs, but much less likely when taken in conjunction with T
    - Discuss that these medications are used for lots of indications, not just birth control!

ADDITIONAL MEDICATIONS

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Contraception across the transmasculine spectrum

Chance Krempasky, FNP-BC, WHNP-BC; Miles Harris, FNP-BC; Lauren Abern, MD; Frances Grimstad, MD, MS

	Invasive/pelvic procedure	Contains estrogen	Contains progesterone	Risk for spotting/bleeding	Reduces/ceases bleeding	Effect on cramping	Chest/breast tenderness	Privacy/concealability	Requires frequent dosing [1]	Clinician needed to discontinue	Efficacy (perfect/typical)
Combined Oral Contraceptives	N	Y	Y	low	If continuous	↓	+ at start	moderate	N	N	99/91
Progesterone Only Contraceptive Pill	N	Y	Y	low	Y	↓		moderate	N	N	99/91
Patch	N	Y	Y	low	If continuous	↓	+ at start	moderate	Y	N	99/91
Ring	frontal insertion	Y	Y	low	If continuous	↓	+ at start	moderate	Y	N	99/91
Depot medroxyprogesterone acetate	N	N	Y	high	Y	↓	infrequent	very	Y	N	99/94
Implant	subdermal insertion	N	Y	high	Y	↓	possible	very	N	Y	99/99 [2]
Intrauterine Device (IUD): Copper	Y	N	N	low	Heavier bleeding	↑	N	very	N	Y	99/99
IUD: Progesterone	Y	N	Y	high	Y	↑ at insertion, then ↓	possible	very	N	Y	99/99
Sterilization	requires surgery	N	N	N	N	none	N	very	N	n/a	99/99
Diaphragm	frontal insertion	N	N	N	N	none	N	moderate	N	N	94/88
Condom: Internal	frontal insertion	N	N	N	N	none	N	low	n/a	N	95/79
Condom: External	N	N	N	N	N	none	N	low	n/a	N	98/82
Emergency Contraception (EC): Ulipristal acetate [3]	N	N	N	Y	N	↑, self-limiting	possible	one dose (prescription)	n/a	N	85/85 [4]
EC: Levonorgestrel	N	N	Y	Y	N	↑, self-limiting	possible	one dose (over the counter)	n/a	N	75-89 [5]

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"MICRODOSING"

- Microdosing: Using low doses or limited doses of testosterone or estrogen to affirm a gender identity.
  - No one way!

  ** Individualized approach

- Pre-prescription counseling is strongly recommended
  - Clear understanding of goals and realistic expectations
  - Discussion of:
    - permanent vs reversible changes
    - unique and unpredictable responses

- Dosing often started low and monitoring closely by patient and provider
  - For affirmation, not necessarily lab values!
- Give/remind about the option to stop hormone therapy whenever the medication is no longer affirming or desired

- Some patients may wish to start on lower than usual doses and slowly increase over time.
  - Giving the option for slowly experiencing the effects of hormones may provide some relief, decreased anxiety, and autonomy over the process
  - This is not a mark of someone's trans-ness!

✦ A safe, but flexible approach to dosing should be presented during the informed consent process for ALL patients when initiating hormone therapy.

ALTERNATIVE USES FOR and OF TESTOSTERONE

- Testosterone cream/DHT cream for clitoral enlargement
  - Sure … but, may not help
  - Consider systemic absorption
  - Compound testosterone cypionate 5% in petrolatum base
  - Can also talk to patients/ask about pumping. Risks vs benefits

- Add-back testosterone following gonadectomy
  - Typically recommended by surgeons or requested by patients following gonadectomy (orchiectomy, vaginoplasty). Particularly if T was not fully suppressed prior to surgery
    - Libido
    - Energy
  - Usually short-term. Many patients decide against it or stop taking on their own after short time
  - Systemic absorption, so potential to cause all of the effects of T — discuss expectations and possibilities
  - Recommend topical — start with small amount (1/4 packet, part of a pump) and can always titrate up
  - Consider progesterone
  - Suppress T prior whenever possible

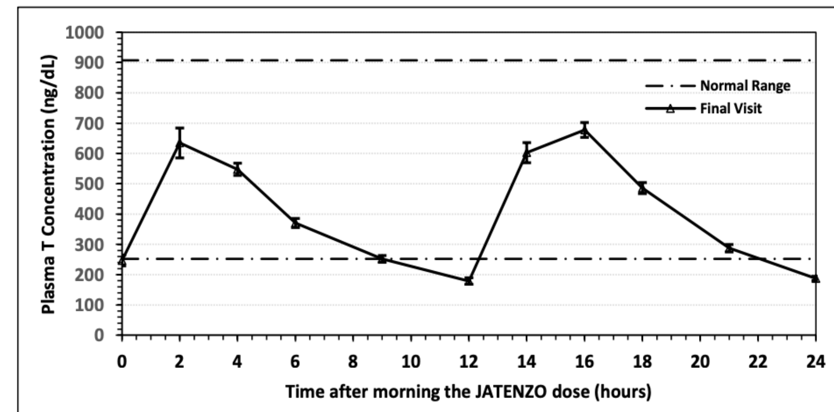
ALTERNATIVE USES FOR and OF TESTOSTERONE

- **Jatenzo**
  - Oral testosterone undecanoate, gel caps
  - FDA approved March 2019
  - 158mg, 198mg, 237mg doses. Recommended 237mg twice daily with food
  - 4mo clinical trial of n=166, 87% of cisgender men achieved therapeutic T levels

JATENZO® CIII
(testosterone undecanoate)
Capsules

Black box warning regarding BP increase, which may increase risk of adverse cardiovascular events

- Most common reactions: headache (8%), Hct increase (8%), HTN (6%), decrease HDL (5%), nausea (4%).
- Also acne, PSA increase, diarrhea, insomnia, mood changes, hyperlipidemia, peripheral edema
- Hepatotoxicity is listed as possible serious reaction, but not black box
- “Prolonged use of high doses of methyltestosterone has been associated with serious hepatic adverse events. JATENZO is not known to cause these adverse events; however, patients should be instructed to report any signs of hepatic dysfunction and JATENZO should be discontinued while the cause is evaluated.”



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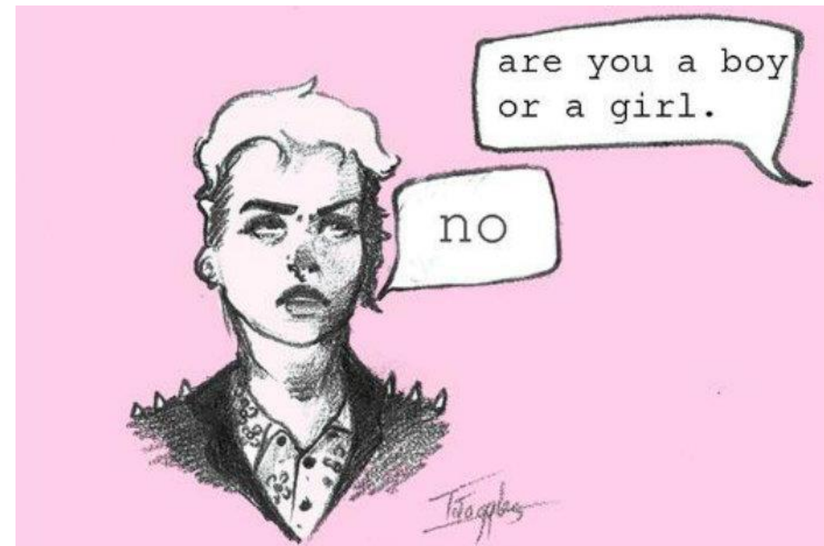
NON-BINARY INDIVIDUALS

- Low/slow dosing
- 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 (at least historically); 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?