NATIONAL LGBT HEALTH EDUCATION CENTER

A PROGRAM OF THE FENWAY INSTITUTE

# TRANSGENDER MEDICAL CARE: ADVANCED CASE DISCUSSION


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## Fenway Health



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- Disclosure: No relevant financial relationships. Content of presentation contains no use of unlabeled and/or investigational uses of products.

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# POLLING QUESTION:
## *Getting to know you*

Check all that apply:

1. I provide clinical care to transgender patients
2. I am not a clinician, but I work in a health care environment that serves trans patients
3. I work or volunteer in a community-based organization that serves trans people
4. I conduct research with trans communities
5. I am a student
6. Other (feel free to type in the Q & A panel what brought you to this webinar)

# CASE #1

## Cardiovascular risk in a transgender woman

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- 56 yo trans woman who has been treated by an endocrinologist in New York for 8 years with injectable estradiol cypionate and oral medroxyprogesterone as well as spironolactone.

- She is a non-smoker with no hx of HTN and reportedly normal cholesterol levels but a family hx that includes a father with a CVA in his 50s, a mother with MI x2 in her 70s, and several secondary relatives with cardiovascular disease.

- She presented to her local emergency room with sx consistent with increasing exertional angina and chest pain at rest for 5 days.
- Her EKG showed ischemic changes and a cardiac cath showed a 95% LAD stenosis; left circumflex and RCA with minimal disease.
- She had a drug-eluting stent successfully placed across the LAD stenosis.

# POLLING QUESTION

- **How would you manage her hormone therapy?** ***Choose one.***

1. Stop all medications
2. Continue all medications (no effect on cv health)
3. Stop the progesterone only
4. Stop the progesterone and switch to transdermal estrogen

- Her cardiologist and her PCP told her to stop all of her hormonal medications, which she did 6 months prior to her current visit with you today
- She presents in great emotional distress, reporting that she feels as though she is beginning to masculinize again, with a change in body proportions and coarsening and increase in body hair

- Currently on rosuvastatin (Crestor), carvedilol, a daily aspirin, and prasugrel (Effient)
- She has had no further episodes of chest pain since her LAD stent was placed

- On exam, she is well-appearing but anxious and intermittently tearful
- P 66  BP 127/80 cardiac exam is normal
- She does demonstrate some dark, coarsened body hair on extremities
- genital exam reveals slightly atrophic testes

- LDL 72  HDL 61
- Total testosterone 471
- Estradiol 10

# RISK/BENEFIT ANALYSIS OF HORMONE THERAPY

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# WOMEN'S HEALTH INITIATIVE STUDY

| | Odds ratio | Increased Incidence |
|---|---|---|
| CHD event | 1.29 | 7/10,000 |
| Non-fatal MI | 1.32 | 7/10,000 |
| CHD death | 1.18 | 1/10,000 |
| PE | 2.13 | 8/10,000 |
| CVA | 1.41 | 8/10,000 |
| DVT | 2.07 | 13/10,000 |

# HERS (HRT IN PATIENTS WITH PRIOR CORONARY EVENT)

- Treatment with conjugated estrogen (Premarin) and steroidal progestin (Provera)
- 1380 patients in treatment and control groups
  - No significant difference in primary outcomes
  - Lower LDL  and higher HDL in treatment group
  - More events in treatment group in year 1, but fewer in years 4 and 5
  - Increased risk of VT ( 32 vs 12 cases)

# ASSCHERMAN, ET AL (2011)

- 996 MtF patients, 18.5 years follow-up
  - current but not past use of ethinyl estradiol (EE) associated with 3x risk of CV death
  - about 2x rate of CV death in 40-64 yo
  - ischemic HD death in 18 subjects, 11 had been using EE, 5 had suffered previous MI
  - stroke in 5 subjects; in younger subjects, all had used EE
  - in over 65 yo, total mortality was not increased
  - higher lipid levels and higher rates of smoking in MtF

# GOOREN, ET AL (2008)

- 2236 MtF patients
  - Increased weight, visceral fat, impaired glucose sensitivity, small increase in BP; increased HDL, decreased LDL
  - NO increased in cardiovascular morbidity or mortality
  - Increased incidence of venous thromboembolism (VT) (6-8%) but only in patients treated with EE

# ELAMIN, ET AL (2010)

- Meta-analysis of 16 eligible studies, 1471 MtF
  - Very few reported cardiovascular events
  - Quality of evidence is very low
  - No meaningful assessment of clinical outcomes like death, stroke, MI or VT
  - SUGGESTS a higher incidence in MtF, BUT most were from one center using “fairly high estrogen dose”

# WILSON, ET AL (2006 AND 2009)

- MtF patients treated with oral and transdermal estrogen
  - increased levels of anti-oxidant and decreased levels of inflammatory markers suggesting cardiovascular BENEFIT
  - Oral estrogen resulted in a transient increase in inflammatory markers and clotting factors (within 2 to 4 months but returning to baseline by 6 months)
  - Transdermal estrogen did not seem to affect inflammatory markers and clotting factors

# TOORIANS, ET AL (2003)

- Chemical measures of coagulability in FtM patients on EE, oral estradiol and transdermal estradiol
- Oral and transdermal estradiol groups were similar in all measures of pro-thrombotic variables, and did not differ in the baseline levels seen in natal females
- An earlier study had shown the incidence of VT was 20 x higher in oral EE versus transdermal estradiol

- Use of progesterone in MtF patients
- WHI study showed increase in cardiac events in those women using combination therapy

- Our patient was started on transdermal estradiol patch 0.1 mg twice a week along with spironolactone

- 4 months after re-starting hormonal treatment, serum estradiol of 123 and total testosterone of 236
- 1 year out, no angina or cardiac events
- Patient is saving money for orchiectomy

# QUESTIONS OR COMMENTS ON CASE #1?

# CASE #2

## Pelvic/genital complaints in a transgender man

- 36 yo trans man on testosterone for 18 months
- Previous history of somewhat irregular menses
- Recent hx of recurrent dysuria along with discomfort with sexual intercourse. Now with intermittent vaginal spotting, usually occurring after sexual intercourse
- Identifies as polyamorous.  5 partners in the past 6 months. Does have penetrative vaginal sex and admits that he occasionally forgets to use condoms

# POLLING QUESTION

**What is the likely diagnosis? *Choose one***

1. Normal ovulatory bleeding
2. Sexually transmitted infection
3. Pregnancy
4. Atrophic vaginitis
5. Fibroid tumor
6. Malignancy

- He has been treated several times for presumptive STD and UTI, but STD testing and urine cultures have been repeatedly negative

- Serum HCG was negative
- Testosterone does not reliably suppress ovulation

- PALM-COEIN
  - polyp, adenomyosis, leiomyoma, malignancy, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, not yet classified
- Cervical:  cervicitis, polyps,vervical CA
- Vaginal:  atrophy, ulcerations, vaginitis, trauma, benign growths, cancer
- Also consider vulvar or anal lesions

- Menses should cease within 6 months of initiating hormone therapy
- Continued ovulatory bleeding may occur despite testosterone treatment
- Ensure that patient is taking medication correctly and consistently
- Can check LH to ensure suppression of HPG axis

- If ovulatory bleeding, consider increase in testosterone dosing or use of progesterone

- Pelvic exam was performed on our patient with some discomfort
- Vaginal mucosa was atrophic with some friability of the vaginal mucosa and cervix
- Bimanual exam was limited
- Pap smear was negative for malignancy and high-risk HPV

- 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 endometrial carcinoma in an FtM patient after 7 years on testosterone tx

- Ultrasound was performed to assess for structural lesions and to evaluate the endometrium

- Our patient's uterine ultrasound was normal: no fibroids, no obvious endometrial polyps,  thin endometrial stripe

- Patient's symptoms were felt to be due to atrophic vaginitis/cervicitis
- Treated with Estring
- Patient's symptoms resolved

- Pelvic pain in transgender men
  - ? testosterone effect on uterine smooth muscle
  - ? local estrogen or prostaglandin effect
  - ? musculo-ligamentous pain
  - consider ovarian pathology

- Sometimes will respond to NSAIDs
- Mirena IUD
- Consider PT referral
- ?? SERMs (raloxifene)
- Not infrequently requires referral to gynecologist and consideration for surgery

# QUESTIONS OR COMMENTS ON CASE #2?

# CASE #3

## Silicone use

## in a transgender woman

- 29 yo trans woman who has been on estrogen therapy and spironolactone for 6 years and is well feminized
- In her late teens, attended “pumping parties” and had, on several occasions,  large volumes of silicone injected into soft tissue over hips and buttocks

- She now presents with painful indurated masses over her bilateral sacral areas; these occasionally become inflamed with pain, overlying erythema and warmth. Sometimes accompanied by malaise, nausea, subjective fevers
- In addition, she experiences intermittent swelling in BLE, worse on right. She also reports swelling and redness in the joints of her lower extremities

- She has had surgical excision of several smaller and more localized nodules over her upper gluteal areas, but has been told that the larger lesions cannot be excised
- Her symptoms have been treated chiefly with NSAIDs
- She notes that the redness and pain have improved with courses of antibiotics, but later flared up again

- On exam, she is relatively thin; in no acute distress
- She has two large (approx 6 x 4 cm) areas of irregular induration without clear borders. At the time of exam, there is no erythema or warmth, but there is some pitting some mild tenderness
- She also has some dusky brown-red discoloration over her right hip
- She has trace to 1+ edema of her distal RLE. Her left ankle has a small effusion, but no erythema or warmth

# POLLING QUESTION

***What percentage of your transgender women patients have used injectable silicone?***

1. None
2. <5%
3. 5-20%
4. >20%
5. Not applicable (I don't see trans women patients)

- For years, transgender women have been known to use non-professional injection of subcutaneous silicone, sometimes mixed with other oils and fillers, sometimes of industrial grade
- Complications first reported in the medical literature in the mid 70s
- Recent media attention (NY Times August 2011) and online discussions

- Acute complications can include pain, redness, induration, infection,  abnormal pigmentation, migration of injected material, embolization
- Severe local tissue reactions with local necrosis and ulceration

- Acute silicone syndrome occurring hours to days after injection
- Dyspnea, cough, chest pain, hypoxia, hemoptysis, alveolar hemorrhage, fever
- Occasional neurologic sx and alteration of consciousness, hepatic, GI  and cardiac involvement
- Treated with steroids (and antibiotics) and may fully recover
- Overall mortality of 24 to 33%; 100% with neurologic sx

- Chronic and recurrent granulomatous pneumonitis may occur
- Case series suggest that patients with HIV infection may be at higher risk

- Late complications:
  - Inflammatory nodules
  - Cellulitis with sterile abscesses
  - Siliconomas
  - Delayed-onset inflammatory nodules
  - Secondary lymphedema
  - Peristent erythema and telangiectasias

- Bacterial biofilms?

- A more diffuse chronic inflammatory illness has also been reported

- Prior exposure to silicone may predispose to hypersensitivity

- Treatment:
  - Antibiotics: tetracycline/minocycline
  - Intralesional steroids (?)
  - topical imiquimod
  - Etanercept
  - tacrolimus
  - allopurinol

- Telanciectasias and small focal siliconomas may be treated with CO2 laser therapy

- Surgical excision of injected material and granulomatous lesions is often extremely difficult or impossible

- Our patient was started on an extended course of minocycline
- 12 weeks out from therapy, she has not had any inflammatory flare-ups

# QUESTIONS OR COMMENTS ON CASE #3?

# POLLING QUESTION

**In natal men, the most common reason for stopping testosterone therapy is:**

1. Erythrocytosis
2. Hepatotoxicity
3. Changes in cardiovascular risk factors (lipids or blood pressure)
4. Mood alterations

# CASE #4

## Erythrocytosis in transgender man

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- 33 yo transgender man who had been on testosterone in the past and then stopped for financial reasons. Re-started testosterone at 100 mg IM weekly
- Baseline Hgb/Hct of 12.1 and 38.2
- 6 months after starting back on hormone tx, testosterone level 1041. Hgb and Hct of 15.7 and 53.4, increasing to 17.3 and 57.2 two months later

- Non-smoker. No history of chronic respiratory or cardiac disease.
- No known family hx of elevated Hgb/Hct
- The patient denied any unusual symptoms. No chest pain, dyspnea, headache, fatigue or neurologic sx
- Exam was unremarkable

- Testosterone dose was decreased although it is not clear that patient was taking the dose intended by the physician
- Hgb and Hct did not improve after a month on lower dose

- Patient was referred to a hematologist.
- Confirmed elevated Hgb/Hct, tested for red blood cell volume, genetic screening, abdominal ultrasound and then MRI
- Patient's erythropoietin level was elevated

- Patient was told by hematologist and by PCP to stop the testosterone with no plan to resume therapy at any point

- Increase in red cell volume is expected “side effect” of testosterone treatment
- In natal men on androgen replacement tx, 6 to 25% see increase in Hct above the normal range

- What is considered normal?
- Upper limit of normal male range is a HCT of 52% (Hgb of 18.)
- Upper limit for females and black males is HCT of 48% (Hgb 16.5)

- Concern is increased blood viscosity and subsequent decreased tissue perfusion and thrombosis
- In men with polycythemia vera, annual incidence of thrombotic events ranges from 1.8% in those under 40 to 5.1% in patients older than 70
- Symptoms may include chest pain, dyspnea, fatigue and lethargy, headaches and neurologic symptoms

- In natal men on testosterone therapy, increased red blood cell volume apparent by 3 months of treatment and peaks at 9 to 12 months
- Older men more likely to develop increased Hgb/Hct and develop symptoms/complications
- More likely to occur with injectable testosterone than with topical formulation

- Recommended treatment for trans men is the same as for natal men: decrease dose or stop testosterone treatment if Hct > 52%
- Initiate therapeutic phlebotomy if Hct > 54%, with a goal of reducing the Hct to 45%

- Our patient had been off testosterone tx for almost 6 months when seen initially. At that time Hgb/Hct were 13.7 and 43.0 with testosterone in the female range

- The patient was started on topical testosterone gel applied daily at 25 mg initially, and then increased to 50 mg daily
- Testosterone level when last checked was in the low end of the male range with a Hct of 45%.

# QUESTIONS OR COMMENTS ON CASE #4?
# GENERAL QUESTIONS?

# RESOURCES

- National LGBT Health Education Center:
  - www.lgbthealtheducation.org
  - Front-line Staff Tool for Gender Affirming Environments
  - Webinars "On Demand"
- Fenway Health Trans Health Program
- Center of Excellence for Transgender Health
- WPATH