#204

Assessing Biologic Risk for HIV Transmission in Transgender Women

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ABSTRACT

Background: High HIV infection rates in transgender women (TGW) are largely attributed to increased behavioral risk factors. However, effects of exogenous hormones on the immune system and injectable fillers or sex reassignment surgery (SRS) on immune activation may alter HIV risk.

Methods: A cross-sectional study of HIV negative volunteers including 10 men who have sex with men (MSM), 10 natal or cis-women (CW) and 8 TGW post SRS was conducted. Peripheral blood mononuclear cells (PBMC) and mucosal mononuclear cells (MMC) isolated from sigmoid biopsies (TGW, MSM, CW), and cervical (CW) and neovaginal (TGW) swabs were analyzed. Lymph node (LN) biopsies underwent immunohistochemical staining.

Results: Median lifetime sexual partners was higher in TGW (53) compared to CW (3, p=0.006) and MSM (25, p=NS). Among TGW, mean age of initial gender dysphoria was 7yrs, cross dressing 13yrs, hormone initiation 14yrs, and SRS 24yrs. Median duration of hormone use in TGW was 7.6yrs, with 5/8 using estrogen/progesterone, and 3/8 estrogen only. Median time post SRS was 1.3yrs, all by penile inversion, with 7/8 still using dilators post SRS. All TGW reported anal sex; 7/8 reported neovaginal sex.

No difference in frequency of CD4+ or CD8+ T cells in PBMC and sigmoid MMC among groups was found. Frequency of neovaginal CD4+ T cells was decreased (1.8%) and CD8+ T cells increased (77.7%) vs. sigmoid and cervical CD4+ (54.4% and 48.3%), and CD8+ (33.6% and 30.2%) T cells (p<0.001, all). Neovaginal CD4+CCR5+ T cell frequency was lower than in cervical MMC (1.2% vs 35%, p=0.02), but comparable to sigmoid MMC (31.1%, p=NS). MFI of CD4+CCR5+ T cells was higher in neovaginal MMC (1491) vs. sigmoid MMC (761, p=0.04), but similar to cervical MMC (578, p=NS). Increased activated CD4+ T cells (HLA-DR+/CD38+), were seen in cervical MMC (2.3%) vs. sigmoid (1.1%) and neovaginal MMC (1.0%, p=0.02 and p=0.05, respectively). Filler use was higher in TGW (63%) than MSM (10%) or CW (0%). One TGW using hip fillers had multiple inguinal siliconomas, corresponding with high frequency of peripheral Ki67+CD4+ expression (0.4% vs median 0.1% in TGW) and Ki67+CD4+ cells in her inguinal LN.

Conclusions: CD4/CD8 T cell composition of neovaginal MMC differs from sigmoid and cervical MMC. There was no increase in frequency of neovaginal activated CD4+ or CD4+CCR5+ T cells. Higher use of fillers in TGW may contribute to systemic immune activation, although studies are ongoing. Characterization of biologic HIV risk factors specific to TGW may inform additional prevention strategies.

BACKGROUND

High HIV prevalence among transgender women (TGW)

- Global TGW pooled HIV prevalence **19.1%** (CI: 17.4-20.7%)
- Odds of HIV+ among TGW vs. all reproductive-age adults:
  - **50.0 times** (CI: 26.5-94.3) in low/middle income countries
  - **46.3 times** (CI: 30.3-70.7) in high income countries

Baral et al., Lancet ID 2013

Possible behavioral causes for discrepant prevalence in TGW

- High rates of psychological issues
- High rates of substance abuse
- Poor access to healthcare

Little is known about differences in HIV susceptibility, acquisition, or control between high risk MSM and TGW, specifically:

- Influence of hormones on CCR5 expression
- Influence of sex-reassignment surgery on neovaginal inflammation
- Influence of systemic fillers on target cell activation

Potential Hormonal Influences on HIV Risk

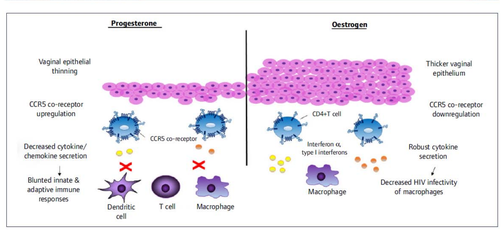


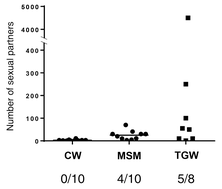
Figure 1. Effects of oestrogen and progesterone on vaginal HIV infection.

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CLINICAL RESULTS

Sexual Risk

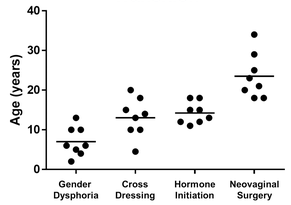
Estimated Lifetime Sexual Partners



Type of Sex

	CW	MSM	TGW
% Vaginal / Neovaginal Only	100	N/A	0
% Anal Only	0	100	13
% Both	0	0	87

Timing of Male to Female Transition



TGW Hormone Use

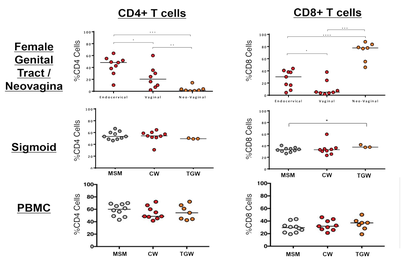
Hormone Use among TGW	8/8
Median (range) duration of hormone use in years	7.6 (0.5 – 16)
Mixed estrogen / progesterone	5/8
Estrogen only	3/8

TGW Surgical History

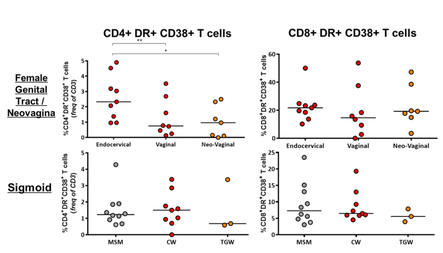
Surgical breast augmentation	7/8
Neovaginal construction via penile inversion	8/8
Neovaginal construction via sigmoidal reconstruction	0/8
Median (range) years post surgery	1.25 (1 – 29)
Use of neovaginal dilators (daily – monthly)	7/8

IMMUNOLOGIC RESULTS

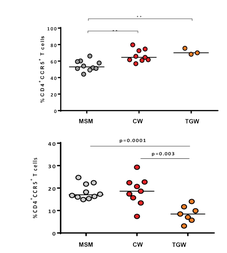
Differential T cell distribution in Female Genital Tract but not in Sigmoid Colon or Peripheral Blood



No Increase in Mucosal T Cell Activation in TGW



Frequency of CD4+ CCR5+ Target Cells in Sigmoid Colon and Peripheral Blood



METHODS

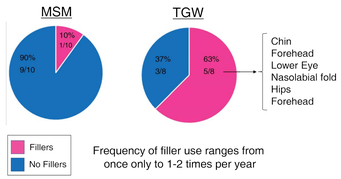
Goal: To determine the biologic effects of hormone replacement therapy and neovaginal surgery on HIV susceptibility

Design:
n=30: 10 cis-women (CW): not taking hormonal contraceptives
10 Men who have sex with men (MSM)
10 Transgender women (TGW):
post sex reassignment surgery

Study Procedures:
Detailed, standardized clinical history
Single cross-sectional collection of blood, cervical / vaginal cells via Floqswab (CW), and neovaginal cells via Floqswab (TGW) in all
Optional inguinal lymph node biopsy and sigmoid biopsy offered to all

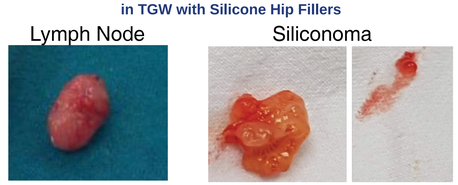
IMPACT OF FILLER USE

Use of Fillers



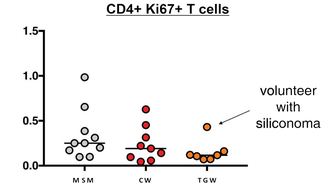
Frequency of filler use ranges from once only to 1-2 times per year

Inguinal Siliconoma Mimicking LN in TGW with Silicone Hip Fillers

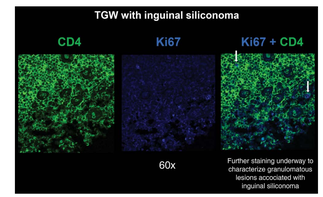


PBMC Activation

CD4+ Ki67+ T cells



Little LN Activation in HIV Negative MSM or TGW



CONCLUSIONS

- Vaginal T cell composition differs between TGW and CW.
- Although systemic and lymph node activation appears similar across groups in this pilot study, there may be an increase in sigmoidal CD4+ CCR5+ target cells for HIV in TGW.
- Additional studies are underway to quantify soluble factors of inflammation in genital secretions, lymph node activation, and microbiome composition across groups.
- These findings support the need to power future efficacy trials to analyze TGW as an independent subgroup, although larger cohort studies are needed.

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