Anal high-risk human papillomavirus (HPV) infection among HIV-infected MSM in the SUN Study, 2004-2011

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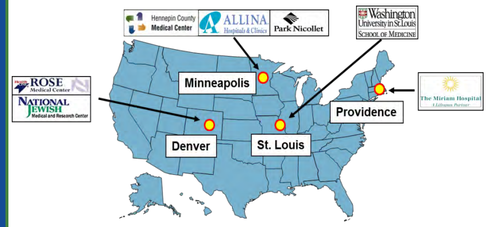
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BACKGROUND

- Incidence and clearance of anal high-risk HPV (HR-HPV) infection in HIV-infected men who have sex with men (MSM) have not been well characterized. These dynamics may have implications for vaccine strategies to reduce anal cancer burden.

Sun Study Design:

- The Study to Understand the Natural History of HIV/AIDS in the Era of Effective Therapy ('SUN' Study) is a closed prospective observational cohort study of 700 HIV-infected patients receiving care at seven clinics in four U.S. cities



- Participants were enrolled from March 1, 2004 to June 30, 2006 and followed every six months until June 1, 2012.
- At enrollment, providers collected anal swabs for HPV detection and genotyping (Roche Linear Assay).
- Participants also completed an audio computer-assisted self-interview regarding demographics and sexual behavior.

METHODS

- Among MSM, we evaluated the baseline prevalence of HPV types 16 and 18 at the anus and incidence and clearance annually over 48 months using Kaplan-Meier survival analysis. For men with prevalent HPV 16 or HPV 18, we defined clearance as two consecutive visits where the respective HPV type was undetected.
- We assessed the associations of prevalent and incident infection, and clearance of prevalent infection, with selected baseline behavioral and clinical characteristics.

RESULTS

- Among 403 MSM, the median age was 42 years; 78% were prescribed HAART; median CD4 cell count was 454 cells/mm3; and 74% had an undetectable viral load. (see Table for characteristics).
- The prevalence of HPV 16 was 38% (n=152) and HPV 18 was 24% (n=97) (p=0.193); 10% (n=42) were co-infected with both HPV types.
- Men who injected drugs were more likely to be infected with prevalent HPV 16 (53% vs. 36%, p=0.024), while men with rectal Neisseria gonorrhea infection (67% vs. 24%, p=0.009), CD4 cell count < 500 cells/mm3 (29% vs. 17%, p=0.004), and ≥ 4 sex partners during the 6 months before baseline (33% vs. 21%, p=0.012) were more likely to be infected with prevalent HPV 18.
- Over 48 months, the incidence of HPV 16 was 23% (95% confidence interval (CI): 18%-30%) and of HPV 18 was 13% (95% CI: 9%-17%).
- Five percent (n=8) had both incident HPV 16 and 18 detected. Anal sex in the 6 months before baseline (31% vs. 14%, P=0.006) and consuming alcohol in 30 days before baseline (25% vs. 10%, p=0.038) were associated with HPV 16; marijuana use in 6 months before baseline was associated with HPV 18 (20% vs. 10%, p=0.021).
- At 48 months, 26% (95% CI: 18%-36%) cleared prevalent HPV 16 and 50% (95% CI: 38%-64%) cleared HPV 18 (Figure).
- In MSM with vs without persistent HPV 16 and 18, squamous intraepithelial lesions were detected in 56% vs 37% (p=0.006), and 68% vs 38% (p=0.003), respectively.
- MSM who reported ever using methamphetamine vs no use were less likely to clear HPV 16 (24% vs 46%, p=0.039).
- Only clearance of prevalent HPV type 16 was associated with unprotected receptive anal sex: 33% of 64 reporting anal sex compared with 56% of 53 who did not, odds ratio 2.65, p=0.004

Figure.

Clearance of high-risk anal HPV type 16 and type 18 infection among HIV-infected MSM

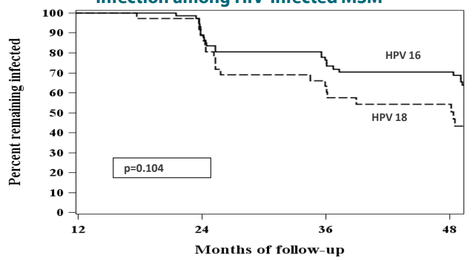


Table.

Selected baseline characteristics for participants from the SUN Study, 2004 – 2006

Characteristic	Men who have Sex with Men n=403 No. (%)
Race/ethnicity	
Non-Hispanic white	304 (75)
Non-Hispanic black	60 (14)
Hispanic	36 (9)
Other/unknown	5 (1)
Median age at baseline (IQR)	42 (36 – 47)
Drug use in last 6 months	
Marijuana	141 (35)
Cocaine	43 (11)
Inhaled nitrates (poppers)	118 (29)
Club drugs, including methamphetamines	30 (7)
Injection drug use	8 (2)
Number of sex partners in last 6 months	
0	72 (18)
1	129 (32)
2 - 3	88 (22)
> 3	113 (28)
Receptive anal intercourse, ever (n=375)	349 (93)
Receptive anal intercourse in last 6 months (n=373)	190 (51)
Used ED* agents in last 6 months	71 (18)
Current cigarette smoking	160 (40)
Nadir CD4+ cell count (cells/mm^3)	
< 50	64 (16)
50 – 199	125 (31)
≥ 200	211 (53)
Median nadir CD4+ cell count (IQR)	209.5 (100 – 326.5)
Baseline CD4+ cell count (cells/mm^3)	
< 200	36 (9)
200 – 349	95 (24)
350 – 500	108 (27)
> 500	161 (40)
Median baseline CD4+ cell count (IQR)	453.5 (311.5 – 655)
Viral load < 400 $\log_{10}$ copies/ml	299 (74)
Antiretroviral-naïve	53 (13)
Current cART	316 (78)
Years on cART (median, IQR)	3.1 (1.2 – 5.9)
Rectal *Neisseria gonorrhoeae* (n=384)	9 (2)
Rectal *Chlamydia trachomatis* (n=379)	31 (8)

Abbreviations: cART, combination antiretroviral therapy; IQR, interquartile range;
* ED=erectile dysfunction agents, including sildenafil citrate, tadalafil, or vardenafil

CONCLUSIONS

- Among HIV-infected MSM with a prevalent HR-HPV infection, 26% with HPV 16 and 50% with HPV 18 cleared by 48 months.
- MSM using methamphetamine may be at higher risk for anal dysplasia and cancer than MSM that do not report use of metamphetamine.

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