



# Genital CMV Shedding Predicts Syphilis Acquisition in HIV Infected MSM on ART

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## Background

- Bacterial sexually transmitted infections (STI) are highly prevalent among HIV infected men who have sex with men (MSM) and are co-factors in HIV transmission.
- While behavioral factors are important in STI acquisition, other biological factors such as immune modulation due to chronic viral infection may also predispose to STI acquisition.

## Primary Objective

- **To determine if asymptomatic genital CMV replication is associated with increased risk of STI acquisition.**

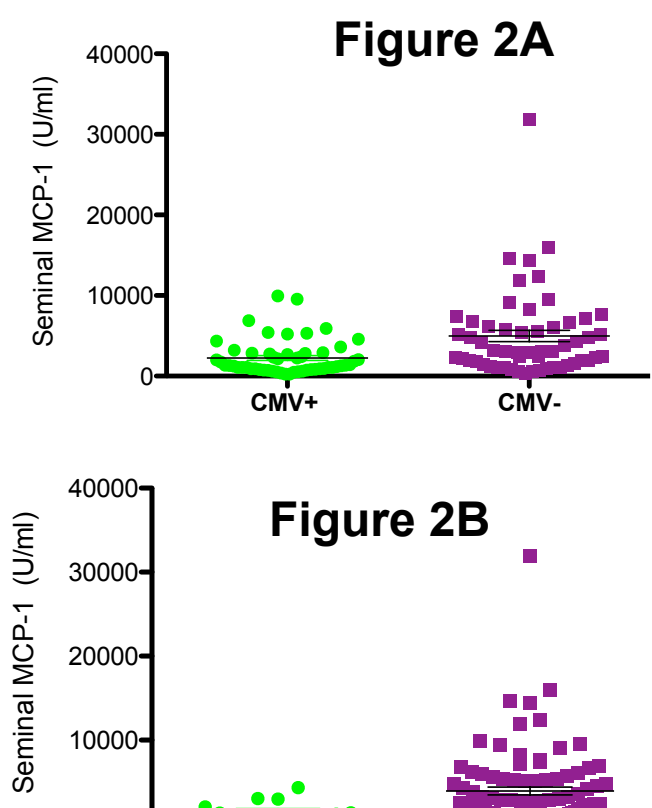
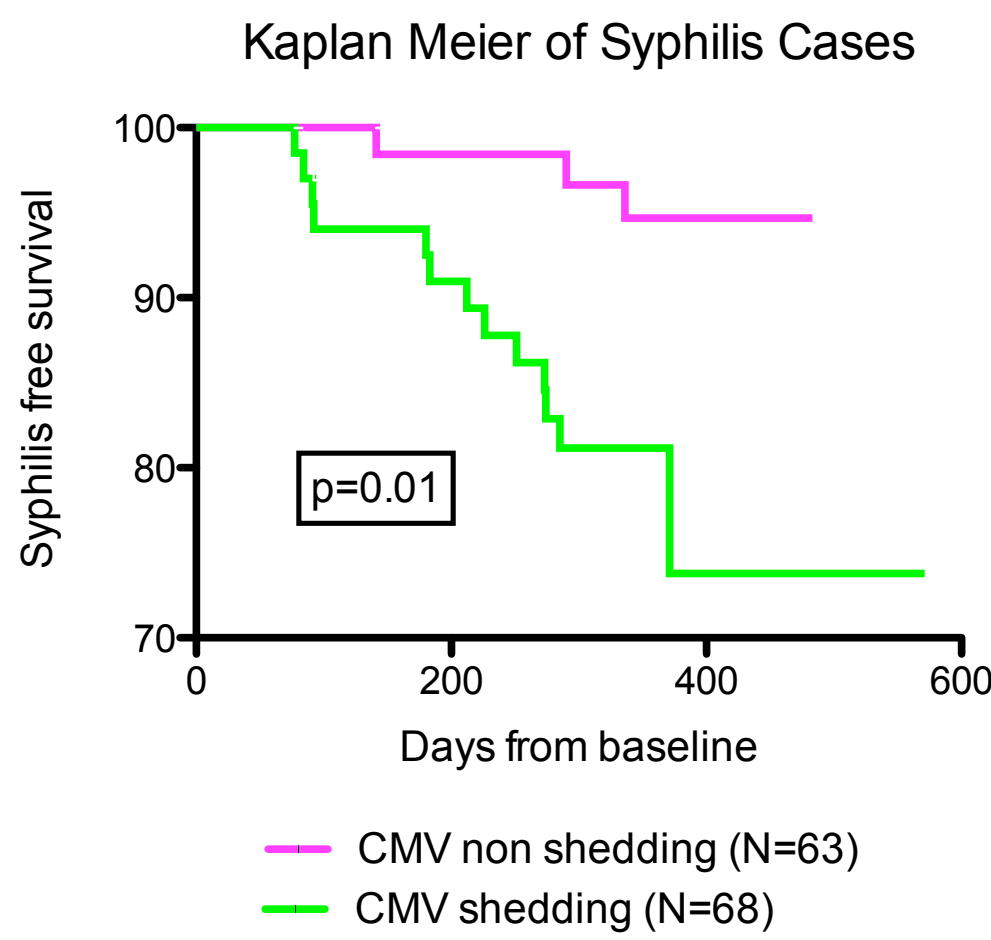
## Methods

- 131 HIV+ MSM on suppressive antiretroviral therapy (ART) were followed for 12 months and screened every 3 months for the following STI:
  - *Neisseria gonorrhoeae* (throat, rectal, and urine by transcription-mediated amplification [TMA]).
  - *Chlamydia trachomatis* (throat, rectal, and urine by TMA).
  - Syphilis (by RPR and TPPA confirmatory tests).
- Baseline predictors of bacterial STI were determined using survival analysis of time to incident STI. Differences between groups were tested by Mann Whitney test.
- Tested variables at baseline included:
  - genital shedding of herpesviruses (CMV, EBV, HSV, HHV-6, -7, and -8) .
  - behavioral factors (# of sex partners, # of anal sex acts, use of methamphetamine and other drugs).
  - Current CD4 T cell count.
  - Markers of genital inflammation (MCP-1, IL-6, TNF- $\alpha$ , Interferon- $\gamma$ , RANTES and IP-10 in seminal plasma).

## Table 1: Factors Associated with Incident Syphilis

Factor	Syphilis; n (%)	HR	P-value	Adjusted HR
Any detectable semen CMV DNA (N=68)	13 (19.1)	4.14	<b>0.03</b>	3.56 (1.00-12.73)
No detectable semen CMV DNA (N=63)	3 (4.8)			
<40 years	8 (22.2)	3.11	<b>0.02</b>	2.50 (0.92-6.77)
≥40 or older	8 (8.4)			
CD4+ T-cells/ $\mu$ l, mean (95% CI)	591.5 (324-735)	1	0.35	
Any detectable HSV-1/HSV-2 DNA	0 (0)	0	0.99	
Any detectable EBV DNA	6 (16.7)	2.27	0.44	
Any detectable HHV-6 DNA	2 (12.5)	3.4	0.28	
Any detectable HHV-7 DNA	3 (27.3)	3.92	0.06	
Any detectable HHV-8 DNA	2 (22.2)	2.05	0.19	
Baseline syphilis	5 (18.5)	1.07	0.26	
Number of male partners past month (>6)	5 (20.8)	2.1	0.18	
Any unprotected anal sex acts past month	5 (9.8)	0.67	0.46	
Any illicit drug use other than marijuana	7 (15.2)	1.54	0.39	

**Figure 1: Kaplan Meier of Syphilis Cases**  
**Figure 2: Levels of seminal MCP-1 among Groups**



**Figure 1:** Presence of CMV shedding was associated with more frequent syphilis acquisition.

**Figure 2:** CMV shedding (panel A) and syphilis acquisition (panel B) were both associated with LOWER seminal MCP-1 levels (Mann Whitney test).

## Results

- All were CMV seropositive and 52% shed CMV in semen at baseline.
- 34 subjects (26.2%) acquired one or more bacterial STI during 12 months of follow-up (16 syphilis, 20 gonorrhea, 14 Chlamydia).
- Acquisition of syphilis during follow-up was associated with genital CMV shedding at baseline (p=0.03), and younger age (p=0.02). In the multivariate model, CMV shedding had an adjusted hazard rate for syphilis acquisition of 3.56 (95%CI: 1.00-12.73). **Table 1 and Figure 1**
- None of the variables except higher number of sexual partners was associated with acquisition of STI other than syphilis (not shown).
- Presence of detectable CMV DNA in semen was associated with lower levels of seminal MCP-1 at baseline (median of 1351 [IQR: 839-2847] vs. 3108 [1570-6722] IU/ml, p=0.0006).
- Lower levels of seminal MCP-1 were associated with syphilis acquisition during follow-up compared to no syphilis (median 1142 [IQR: 819-2046] vs. 2436 [IQR: 1084-5339] IU/ml, p=0.01). **Figures 2A and 2B.**

## Conclusions

- **This prospective study demonstrated that CMV shedding in semen is associated with syphilis acquisition, but not other STI.**
- **CMV-associated decrease in seminal MCP-1 levels might predispose MSM to syphilis acquisition.**
- **Future studies should determine underlying mechanisms and if a causal association exists.**

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