High Prevalence of Anorectal Chlamydial Infection in HIV-Infected Men Who Have Sex with Men in Switzerland

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Human immunodeficiency virus (HIV)–infected men who have sex with men (MSM) were enrolled in an anorectal *Chlamydia trachomatis* screening study. Anorectal *Chlamydia* DNA was detected in 16 (10.9%) of 147 men, mainly among asymptomatic patients and patients having >20 sexual partners. These results support routine anorectal *Chlamydia* screening in HIV-infected MSM who report unprotected anal intercourse.

In several Western countries, including Switzerland, an increasing proportion of new human immunodeficiency virus (HIV) infection is occurring in men who have sex with men (MSM). Concomitantly, several European countries have recorded a recent, substantial increase in the number of reported sexually transmitted diseases (STDs), particularly among MSM [1]. STDs, including nonulcerative, frequently asymptomatic infections such as *Chlamydia trachomatis* infection, are associated with a several-fold increased likelihood of acquiring HIV infection [2, 3]. Anorectal chlamydial infection might thus be a contributor to the uncontrolled HIV epidemic among MSM. The aim of this study was to determine the prevalence and clinical characteristics of anorectal chlamydial infection in HIV-infected MSM who were followed up in the Swiss HIV Cohort Study (SHCS) [4] and to evaluate the feasibility of anorectal STD screening in routine HIV care.

Methods. Participants were enrolled in the SHCS, which involves a standardized follow-up visit every 6 months that includes questions about sexual activity and condom use [5]. From 1 April 2007 through 31 March 2008, consecutive MSM participants who reported ⩾1 episode of unprotected receptive anal intercourse in the previous 2 years and/or symptoms of proctitis (rectal pain and/or discharge, cramps, bloody stools, or new onset and/or unusual constipation) were invited to be tested for anorectal chlamydial infection. All participants gave written, informed consent, and the study was approved by the ethics committees of participating SHCS centers.

A standardized questionnaire was used to record the following: (1) sexual behavior (including use of sex toys, fisting, oro-anal contact, and trading sex for money), (2) number of sex partners within the previous 2 years, (3) knowledge of partner's HIV serostatus, (4) history of STD, and (5) anorectal, urogenital, or systemic symptoms at the time of the visit. Data on demographic characteristics, CD4 cell count, HIV viral load, current antiretroviral therapy, syphilis, hepatitis B virus infection, and hepatitis C virus infection were retrieved from the SHCS database. Study physicians were provided with kits that contained the questionnaire, a sterile dry cotton-tipped swab (Eurotubo; Deltalab), a sterile tube containing 500 μl of DNA-free water, and detailed instructions. Specimens were obtained by the treating physician by passing the swab 3–4 cm into the anal canal and by rubbing the swab against the anal wall with a rotating motion for 30 seconds. Anorectal cells were exudated from the swab by pressing the swab inside the DNA-free water tube.

All specimens were processed at the Institute of Microbiology in Lausanne. Samples were screened for the presence of *C. trachomatis* DNA by means of a TaqMan real-time polymerase chain reaction (PCR) assay that targeted the cryptic plasmid of *C. trachomatis*, as described elsewhere [6]. This validated assay also detects strains that contain a recently identified 350 bp deletion in the cryptic plasmid [7], because the 71 bp DNA fragment amplified is located 93 bp downstream from the deletion. Positive samples were genotyped by partial amplification and sequencing of the *C. trachomatis ompA* gene fragments, as described elsewhere [8]. Obtained sequences were compared

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Table 1. Risk Factors Associated with Anorectal *Chlamydia trachomatis* Infection among 147 Male Homosexual Participants in the Swiss HIV Cohort Study

Variable	With anorectal *C. trachomatis* infection (n = 16)	Without anorectal *C. trachomatis* infection (n = 131)	OR (95% CI), by univariate analysis	P
Medical history and clinical characteristics				
Age, median years (IQR)	39.5 (32–47)	42 (27–65)	0.75 (0.39–1.41)[a]	.39
Median CD4 cell count	529 cells/μL	459 cells/μL	0.35 (0.03–3.59)[b]	.37[b]
HIV-1 RNA <40 copies/mL	11 (69)	77 (59)	0.36 (0.21–1.97)	.44
Current combination antiretroviral therapy	13 (81)	93 (71)	1.77 (0.47–6.56)	.55
Drug use[c]	5 (31)	38 (29)	1.11 (0.36–3.41)	.85
Alcohol misuse[d]	5 (31)	51 (39)	0.71 (0.23–2.17)	.59
Hepatitis C seropositivity	2 (13)	10 (8)	1.83 (0.36–9.27)	.36
Chronic hepatitis B infection	0 (0)	9 (7)		.59
Concurrent proctitis symptoms	3 (19)	25 (19)	0.97 (0.25–3.69)	>.99
Concurrent urogenital symptoms	1 (6)	12 (9)	0.66 (0.08–5.45)	>.99
History of STDs	11 (69)	88 (67)	1.07 (0.35–3.28)	.89
Chlamydial infection	4 (25)	31 (24)	1.07 (0.32–3.57)	>.99
Gonorrhea	5 (31)	58 (44)	0.57 (0.18–1.73)	.32
Syphilis[e]	9 (56)	55 (42)	1.77 (0.62–5.06)	.28
Sexual behavior and practices within previous 2 years				
Median no. of partners (IQR)	22 (10–100)	6 (2–13)	1.01 (1–1.02)[f]	.002
>20 sex partners	8 (50)	17 (13)	5.64 (1.86–17.09)	.001
Intercourse with HIV-infected partner(s) or declines to answer	14 (88)	92 (70)	2.96 (0.64–13.67)	.23
Consistent condom use with occasional partner[g]	8 (50)	51 (39)	0.63 (0.22–1.80)	.39
Any anal insertive sex	11 (69)	79 (60)	1.44 (0.47–4.40)	.51
Any oral insertive sex	13 (81)	84 (64)	2.42 (0.65–8.94)	.26
Any vaginal insertive sex	1 (6)	4 (3)	2.11 (0.22–20.19)	.44
Any oral receptive sex	14 (88)	102 (78)	1.99 (0.42–9.26)	.52
Being fisted	1 (6)	15 (11)	0.51 (0.06–4.18)	>.99
Use of anal toys	7 (44)	33 (25)	2.30 (0.79–6.69)	.12
Oro-anal contact	9 (56)	71 (54)	1.08 (0.38–3.09)	.88
Ever exchanged money for sex	1 (6)	14 (11)	0.55 (0.06–4.54)	>.99

NOTE. Values shown are no. (%) of patients, unless otherwise indicated. CI, confidence interval; HIV, human immunodeficiency virus; IQR, interquartile range; OR, odds ratio; STD, sexually transmitted disease.

[a] Per 10-year increase in age.
[b] <200 cells/μL vs $\geqslant$200 cells/μL.
[c] Injection or noninjection drug use within the previous 6 months.
[d] Daily consumption of $\geqslant$30 g alcohol.
[e] Positive serum *Treponema pallidum* hemagglutination assay.
[f] Per 1 sex partner increase, within the previous 2 years.
[g] Always used condoms with occasional partners during the previous 6 months.

with *Chlamydia* GenBank sequences for serovar identification. In addition, the presence of *Neisseria gonorrhoeae* DNA was investigated in all specimens by means of a specific homemade TaqMan PCR assay that targeted the 5′ region of the *porA* gene with the following primers and probes: NgF 5′ CGAAGTCAA AGCTGGTGTGG, NgR 5′ TAACTGTATTGCCCGTTTGAC CTT, and NgS 5′ VIC CAGTTGACCGAGCCAC– MGB at concentrations of 200 nmol (primers) and 100 nmol (probe). This homemade PCR assay exhibits an excellent specificity, as shown by the fact that no amplification was detected when testing 10 ng of DNA extracted from various bacterial species: *Neisseria lactamica, Neisseria meningitidis, Neisseria subflava, Neisseria weaveri, Enterococcus faecalis, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus* species, and *Streptococcus pyogenes.*

Demographic data and risk factors were compared between patients with and patients without *C. trachomatis* infection by the Pearson χ^2 test (or the Fisher exact test when indicated) for categorical variables. For continuous variables, medians were compared by the Wilcoxon-Mann-Whitney test. Multivariate logistic regression was performed to identify factors independently associated with *C. trachomatis* infection. All analyses were performed using Stata, version 10 (StataCorp).

Results. Very few patients declined to be screened, and the anorectal swabbing procedure was found to be acceptable and minimally discomforting by all study participants. Of 157 specimens received in the laboratory, 10 were rejected because of either protocol violation ($n = 6$), missing questionnaire ($n = 2$), or noninterpretable result due to presence of PCR inhibitors ($n = 2$). The final analysis thus included 147 anal specimens obtained from 147 participants, with the following characteristics: white race, 93%; median age, 42 years (range, 22–72 years); at least high-school education, 93%; median CD4 cell count, 459 cells/μL (interquartile range, 332–676 cells/μL); receipt of antiretroviral therapy, 72%; HIV-1 RNA <40 copies/mL, 60%; illicit or recreational drug use, 29%; and history of STD, 67% (Table 1).

Anorectal *C. trachomatis* DNA was detected in 16 (10.9%) of the 147 specimens (95% confidence interval [CI], 6.2%–17.6%) and *N. gonorrhoeae* DNA in 4 (2.7%; 95% CI, 0.9%–7.3%). No participant had concomitant *C. trachomatis* and *N. gonorrhoeae* infection. There was 1 lymphogranuloma venereum (LGV) serovar. The non-LGV serovars included G ($n = 5$), J ($n = 4$), E ($n = 2$), and D ($n = 1$). Serovars could not be determined in 3 samples because of very low bacterial loads (threshold cycles between 37 and 40.4). Current proctitis symptoms were reported by 28 participants; infection with *C. trachomatis* was found in 3 participants, and *N. gonorrhoeae* was found in 1 of these. The participant with anorectal LGV had a 7-day history of rectal discharge, cramps, and bloody stools. He had a history of *C. trachomatis* proctitis and syphilis and reported >60 partners during the previous 2 years.

Table 1 shows the characteristics of patients with ($n = 16$) and those without ($n = 131$) anorectal chlamydial infection. Proctitis symptoms were not associated with chlamydial infection. Having >20 sex partners within the previous 2 years was reported by 8 (50%) of the 16 participants with chlamydial infection, compared with 17 (13%) of the 131 participants without chlamydial infection. In a model adjusted for age (per 10 years), insertive anal intercourse, and inconsistent condom use, the odds ratio of anorectal *C. trachomatis* infection was 5.52 (95% CI, 1.78–17.11) for participants with >20 partners within the previous 2 years. There was a trend ($P = .12$) toward anal toy use being associated with anorectal chlamydial infection.

Discussion. The main finding of our study is a high prevalence of anorectal *C. trachomatis* infection among HIV-infected MSM in Switzerland who report unprotected sexual activity, most of whom presented for routine HIV care. The high prevalence together with a strong association with multiple sex partners and their presumed potential for facilitating HIV transmission suggest a possible role for anorectal chlamydial infection in sustaining the ongoing HIV epidemic among MSM in Switzerland. Consistent with prior reports [9], most anorectal chlamydial infections were asymptomatic, indicating the need for increased awareness of these infections among HIV-infected MSM. Our findings underscore a potential role for expanded rectal chlamydial screening in the reduction of the number of new HIV infections among MSM, a group for whom increased HIV prevention efforts are particularly needed. Early detection and treatment of curable STDs was already recommended in a 1998 report by the United States Centers for Disease Control and Prevention (CDC) that also highlighted the importance of asymptomatic infection [3]. Moreover, the CDC recommends at least annual screening for rectal STDs in MSM who report receptive anal intercourse [10].

Our findings are consistent with the high rectal chlamydial infection rate among MSM with newly diagnosed HIV infection in San Francisco [11] and may be related to increased sexual risk-taking behavior among MSM in the era of antiretroviral therapy. In contrast, only one participant had LGV, consistent with the low rectal LGV rate in patients at STD clinics in the United Kingdom [12]. This argues against anorectal LGV being a major driver of the recent doubling of the number of new HIV infections among MSM in Switzerland.

In our data set, the only risk factor for anorectal chlamydial infection was the number of sex partners in the previous 2 years. Detection of additional associations with specific sexual practices presumably was limited by the fact that participants were selected for unprotected anal intercourse, a marker for high-risk sexual activity.

In contrast to previous studies that investigated anorectal chlamydial infection among patients at STD clinics [12, 13], most participants in our study presented for routine HIV care to SHCS-affiliated physicians and were consecutively enrolled on the basis of a single, simple screening question (unprotected anal intercourse in the previous 2 years). We therefore believe that our data represent the current epidemiology of anorectal chlamydial infection in a population representative of sexually active HIV-infected MSM in Switzerland. In conclusion, regular anorectal chlamydial screening should be strongly considered in all HIV-infected MSM who report unprotected anal intercourse, irrespective of symptoms. Additional studies should address the incidence of other anorectal STDs in high-risk HIV-infected MSM, the appropriate frequency of screening, and the indication to screen for other STDs in this setting.

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