Screening of Oropharynx and Anorectum Increases Prevalence of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* Infection in Female STD Clinic Visitors

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Background: The relevance of screening of oropharynx and anorectum in addition to endocervical tests for detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infection is unclear in women, while there is a documented benefit of this approach in men who have sex with men.

Methods: Female visitors to the sexually transmitted disease (STD) clinic were asked about their sexual practice as a part of the routine electronic patient file. In addition to tests for endocervical infection, swabs were taken from the oropharynx and anorectum to test for *C. trachomatis* and *N. gonorrhoeae* based on the history of sexual contact. Routinely, all electronic patient files are anonymously included in a database for surveillance purposes. In this observational study, we analyzed all consultations in the database over an 18 months period.

Results: A total of 4299 consultations were registered; 10% of women had endocervical chlamydia and 1.1% had gonorrhea. The detection rates for *C. trachomatis* and *N. gonorrhoeae* from oropharyngeal samples were 1.9% and 0.8%, and from anorectal samples 8.7% and 1.7%, respectively. Except for 2 cases of pharyngeal gonorrhea, all oropharyngeal and anorectal infections were asymptomatic. Inclusion of oropharyngeal and anorectal tests in the screening protocol was associated with a percentage increase in prevalence of chlamydia by 9.5% and gonorrhea by 31%, relative to tests for endocervical tests alone. The percentage increase in prevalence was higher than that for the symptom-based approach (3.7% and 10.4%, respectively).

Conclusions: Inclusion of oropharyngeal and anorectal tests in the STD screening protocol increases the prevalence of chlamydia and gonorrhea in women. Screening of anatomical sites based on sexual history is preferred over a symptom-based protocol.

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Chlamydia trachomatis and *Neisseria gonorrhoeae* are the most prevalent bacterial sexually transmitted diseases (STD) worldwide. Many countries have implemented national screening programs to decrease the burden of STD and to improve physical and sexual health. In the Netherlands, the national screening program is conducted by 8 regional STD clinics that offer free and anonymous consultation and testing. Screening of high-risk populations has been shown to be feasible and is associated with reduction in the incidence of STD.[1,2]

Various guidelines have been published on screening for *C. trachomatis* and *N. gonorrhoeae* infection in women. The 2006 United Kingdom National Screening and Testing Guidelines consider testing of a vaginal or endocervical sample as the core component of screening for chlamydia and gonorrhea in women.[3,4] In addition, if indicated by sexual history, anorectal and oropharyngeal tests are advised in case of genital discharge or site-specific symptoms.[5] The Centers for Disease Control and Prevention have published similar guidelines that do not include multiple anatomical testing for asymptomatic women.[6] The guidelines of the Dutch Society for Dermatology and Venereology recommend testing of anorectal samples in case of exposure or symptoms of proctitis, and testing for oropharyngeal gonorrhea in case of reported fellatio.[7] Testing for oropharyngeal chlamydia is considered optional.

Various studies among men who have sex with men (MSM) have shown that there is a significant increase in detection of chlamydia and gonorrhea when oropharyngeal and anorectal samples are tested in addition to the routine testing of a urine or urethral sample.[8–13] In fact, in some studies urethral coinfection was only present in a minority of MSM with oropharyngeal or anorectal *C. trachomatis* and *N. gonorrhea* infection.[9,12] Although anatomical site-specific screening for chlamydia and gonorrhea is well-accepted practice in MSM, the value of routine testing of oropharyngeal and anorectal samples from women is unclear. Limited observational data suggest a considerable prevalence of oropharyngeal and anorectal infection, but the number of women included in these studies is low.[14–16] To our knowledge, no systematic studies have been published on the contribution in prevalence of testing oropharyngeal and anorectal samples in addition to an endocervical or vaginal sample in women. If testing of multiple anatomical sites would be determined feasible, this would directly affect screening guidelines. In this study, we evaluate the contribution of oropharyngeal and anorectal tests to routine endocervical tests for the detection of *C. trachomatis* and *N. gonorrhea* infection in a large cohort of female STD clinic visitors.

MATERIALS AND METHODS

Study Population

The STD Clinic in The Hague offers free and anonymous STD screening to people living in the city of The Hague and the surrounding region. The primary focus is on clients with high risk of STD: report of possible STD-related symptoms, MSM, commercial sex workers, men and women <25 years of age, those with more than 3 sexual partners during the 6 months before consultation, and immigrants from countries with high HIV prevalence. After counseling, clients are routinely tested for chlamydia, gonorrhea, syphilis, hepatitis B virus, and HIV. Microscopy of vaginal discharge and urethral smears and other microbiologic tests are done when clinically indicated.

Anatomical Site-Specific Testing for Chlamydia and Gonorrhea

Tests for urethral, oropharyngeal, and anorectal infection were routinely obtained on the basis of sexual history as per routine protocol during consultation. Self-collected vaginal swabs were obtained from asymptomatic women according to standard recommendation, and endocervical samples were collected from those with signs or symptoms suggestive of STD. If fellatio was reported, oropharyngeal swabs were obtained by wiping the swab twice over the lateral posterior sides of the pharyngeal wall followed by wiping once across the pharyngeal wall. An anorectal sample was obtained from women reporting anorectal intercourse by introducing a swab approximately 5 cm into the rectum under rotating movements.

Data Collection

In this cross-sectional study, we analyze all consultations recorded during an 18 months period (January 2007–July 2008). It is a routine practice at STD centers in the Netherlands to complete a standard questionnaire during each consultation as a part of the anonymous electronic patient file. This questionnaire includes questions about sexual preference, presence of symptoms, site of sexual contact, number of sexual partners, and history of STD. Results of all microbiologic tests and treatment if applicable are also recorded. Upon completion of the consultation (including treatment of STI during follow-up visit if appropriate), all files are transferred anonymously into a national web-based database (SOAP) for surveillance purposes. For this study, we retrieved data of our clinic from this SOAP database.

Clinical Definitions

We defined endocervical chlamydia and gonorrhea as a positive test for *C. trachomatis* or *N. gonorrhoeae* for an endocervical swab or self-collected vaginal swab. Change in vaginal discharge, intermenstrual bleeding, or per vaginam blood loss after sexual contact are defined as symptoms of endocervical infection. Oropharyngeal *C. trachomatis* or *N. gonorrhoeae* infection was considered symptomatic in case of a reported sore throat. Anorectal *C. trachomatis* or *N. gonorrhoeae* infection was defined symptomatic when anorectal discharge, blood or slime on the stools, tenesmus, or rectal pain was reported.

Laboratory Tests

Specific vaginal, endocervical, oropharyngeal, and anorectal swabs were used for specimen collection (APTIMA; Gen-Probe Incorporated, San Diego, CA). Samples from each body site were collected in separate sample collection tubes. Testing of samples for *C. trachomatis* and *N. gonorrhoeae* rRNA was done using the APTIMA Combo 2 (AC2) assay (Gen-Probe Incorporated, San Diego, CA) according to the manufacturer's instructions. Genotyping for specific detection of the lymphogranuloma venereum strain was done of DNA from all anorectal samples with positive results for *C. trachomatis*.[17]

TABLE 1. General Characteristics of Study Population

Characteristic	Women
Consultations	4299
Age	24 yr (13–72 yr)
Reported no. sexual partners during past 6 mo	2 (0–1800)
History of STD	514 (12)
Commercial sex-worker	191 (4.5)
Symptoms suggestive of STD	1145 (27)
Chlamydia trachomatis infection	475 (11)
Endocervical infection	434 (91)
Oropharyngeal infection	71 (15)
Anorectal infection	76 (16)
Neisseria gonorrhoeae infection	63 (1.5)
Endocervical infection	48 (76)
Oropharyngeal infection	30 (48)
Anorectal infection	15 (24)
Infectious syphilis	3 (0.1)
HIV*	6 (0.1)

Data are provided as numbers (%) in case of dichotomous variables and as median (range) for continuous variables. Denominator of the percentages of endocervical, oropharyngeal, and anorectal *C. trachomatis* and *N. gonorrhoeae* infection is the total number of infections by that pathogen.
*These data include both clients with known HIV-infection before consultation and those diagnosed with HIV during their visit to the STD clinic.
STD indicates sexually transmitted disease; HIV, human immunodeficiency virus.

Statistical Methods

Data were analyzed using SPSS version 15.0 (SPSS Inc, Chicago, IL) and described as number (%), mean (range), median (range), and proportion. The Mann-Whitney *U* test was used for comparison of continuous variables and the Chi-square or Fisher exact test, if appropriate, for categorical variables when comparing patients with single versus multiple site infections. Screening strategies were compared by calculating the difference in number of cases of chlamydia and gonorrhea detected by 3 strategies: (1) tests for endocervical infection alone, (2) additional screening of oropharynx and anorectum based on reported signs and symptoms, and (3) additional screening of anatomical sites based on reported site(s) of sexual contact. The increase in number of cases detected by the second and third strategy was expressed as percentage increase in prevalence (95% confidence interval [CI]) of chlamydia and gonorrhea relative to the prevalence obtained by tests for endocervical infection alone.

RESULTS

Characteristics of Study Population

During the study period, 4299 visits by women were registered. Characteristics of the study population are summarized in Table 1. The overall prevalence of *C. trachomatis* infection was 11% and *N. gonorrhoeae* infection was 1.5%.

TABLE 2. Distribution of *C. trachomatis* and *N. gonorrhoeae* Infection by Anatomic Site in Relation to Number of Sites Tested Among Women

Anatomic Site(s) Tested	Number (%) Positive for Chlamydia	Number (%) Positive for Gonorrhea
3 sites tested (n = 850)		
Cervical only	16 (1.9)	1 (0.1)
Oropharynx only	7 (0.9)	2 (0.2)
Anorectum only	16 (1.9)	2 (0.2)
Cervical and oropharynx	1 (0.1)	3 (0.4)
Cervical and anorectum	51 (6.0)	8 (0.9)
Cervical, oropharynx, and anorectum	8 (0.9)	3 (0.4)
2 sites tested (n = 2921)*		
Cervical only	260 (9.0)	13 (0.5)
Oropharynx only	17 (0.6)	9 (0.3)
Anorectum only	0	2 (0.8)
Cervical and oropharynx	37 (1.2)	13 (0.4)
Cervical and anorectum	1 (4)	0
1 site tested (n = 528)		
Cervical only (n = 523)	60 (11.5)	7 (1.3)
Oropharynx only (n = 4)	1 (25)	0
Anorectum only (n = 1)	0	0
Total (n = 4299)	475 (11)	63 (1.5)

*Tests for cervical and oropharyngeal infection were obtained from 2896 women and for cervical and anorectal infection from 25 women.

Seventy-six women had anorectal chlamydia; none of them had infection with the lymphogranuloma venereum strain.

Chlamydia and Gonorrhea per Anatomical Site

Oropharyngeal swabs were obtained for 3750 women (87%) and anorectal swabs for 876 (20%) based on report of fellatio and anorectal intercourse. The detection rate of *C. trachomatis* per anatomical site was as follows: cervix, 10%; oropharynx, 1.9%; and anorectum, 8.7%. Positive test results for *N. gonorrhoeae* were obtained from the cervix in 1.1%; oropharynx, 0.8%; and anorectum, 1.7%. In total, 512 women (11.9%) were diagnosed with chlamydia and/or gonorrhea at any anatomical site, including 26 with dual infection. The distribution of *C. trachomatis* and *N. gonorrhoeae* infection by anatomical site is summarized in Table 2. *C. trachomatis* infection involved a single anatomical site in 75% of women with chlamydia, while *N. gonorrhoeae* involved a single site in 57% of cases of gonorrhea. The majority of women with oropharyngeal chlamydia (69%) and gonorrhea (59%) had concurrent infection of other anatomical sites. Also, most women with anorectal *C. trachomatis* (90%) or *N. gonorrhoeae* (73%) infection had multiple anatomical site infection. No significant differences were observed between chlamydia and gonorrhea patients with single versus multiple site infections for age, reported number of sexual partners during the 6 months before consultation, history of STD, or commercial sex work.

Clinical Presentation

The majority of cases of cervical chlamydia (63%) and gonorrhea (54%) were asymptomatic and symptoms of cervicitis had a low positive predictive value for cervical *C. trachomatis* (15%) and *N. gonorrhoeae* (2.1%) infection. Four women reported pharyngitis and 2 of them had oropharyngeal gonorrhea. However, all women with oropharyngeal chlamydia (n = 71) and 28 of 30 (93%) of women with oropharyngeal gonorrhea did not report symptoms of pharyngitis. All cases of anorectal *C. trachomatis* and *N. gonorrhoeae* infection were asymptomatic. Three women reported symptoms of proctitis, but anorectal tests for chlamydia and gonorrhea were negative. Interestingly, symptoms of cervicitis were reported by 9 of 25 women with isolated pharyngeal chlamydia and 2 of 11 women with gonorrhea only detected from the oropharynx. Similarly, 7 of 16 women with isolated anorectal chlamydia and 1 of 4 women with single-site anorectal gonorrhea presented with symptoms of cervicitis only. Altogether, the majority of endocervical, oropharyngeal, and anorectal infections were asymptomatic.

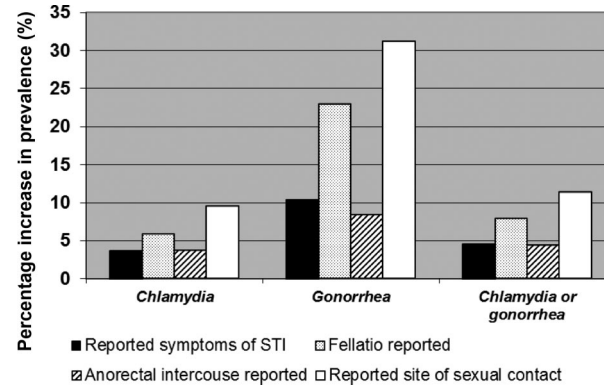

Figure 1. Percentage increase in prevalence of chlamydia and gonorrhea by different strategies of screening of oropharynx and anorectum relative to endocervical testing alone. The following strategies are shown: (1) anatomical site-specific tests obtained if symptoms of cervicitis, pharyngitis, or proctitis are reported, (2) oropharyngeal tests obtained if fellatio is reported, (3) anorectal tests obtained in case of report of anorectal intercourse, and (4) anatomical site-specific tests obtained based reported site of sexual contact.

Comparison of Different Testing Strategies

Figure 1 illustrates the percentage increase in prevalence of *C. trachomatis* and *N. gonorrhoeae* infection that would be obtained by implementation of 4 different screening strategies compared with only testing of endocervical samples. Screening of multiple anatomical sites based on reported symptoms (any of cervicitis, pharyngitis, or proctitis) would increase the prevalence of chlamydia by 3.7% (CI, 3.5%–3.9%) from 10.1% to 10.5%, and of gonorrhea by 10.4% (CI, 10.3%–10.5%) from 1.1% to 1.2%. In all except 2 cases (37/39), the oropharyngeal and anorectal samples would be obtained because of reported cervicitis and not because of reported pharyngitis (n = 2) or proctitis (n = 0). The combination of oropharyngeal and anorectal tests based on sexual history was associated with an 11.3% (11.0%–11.6%) increase in prevalence of chlamydia and gonorrhea from 10.7% to 11.9%. Especially the 31% (CI, 30%–32%) increase in cases of *N. gonorrhoeae* infection from a prevalence of 1.1% to 1.5% by multiple anatomical site testing is of note, while the prevalence of *C. trachomatis* infection increased by 9.5% (CI, 9.2%–9.8%) from 10.1% to 11.0% with the inclusion of oropharyngeal and anorectal tests.

DISCUSSION

This cross-sectional study shows that screening of oropharynx and anorectum based on sexual history results in an

increased prevalence of *C. trachomatis* and *N. gonorrhoeae* infection in women. Unlike in MSM for whom testing of samples of oropharynx and anorectum is part of routine STD screening, there are only limited data on the usefulness of this strategy in women.[14–16] To our knowledge, this is the first large cohort study to evaluate the contribution of oropharyngeal and anorectal tests to endocervical tests on the detection of chlamydia and gonorrhea in women.

Anorectal tests had a much higher detection rate for *C. trachomatis* and *N. gonorrhoeae* than oropharyngeal samples. However, the majority of women with anorectal infection had concurrent endocervical infection and only 20% of women had anorectal tests done. It is questionable whether single-site rectal *C. trachomatis* and *N. gonorrhoeae* infections are a common phenomenon in women. First, concurrent infection of rectum and endocervix is likely to be present due to the close anatomical relation and possible auto-inoculation, which may occur even in women who do not engage in anal intercourse.[13] Second, a proportion of women with single-site anorectal infection may have false-negative results for endocervical sampling. Some of the women with isolated anorectal infection presented with symptoms of cervicitis, but this could also have been caused by pathogens other than *C. trachomatis* and *N. gonorrhoeae*. In that case, obtaining anorectal tests would indirectly increase the detection of endocervical infection that would be missed by routine testing. Finally, it has been suggested that certain serovars are more prevalent in endocervical infection while other serovars may be more associated with anorectal infection.[18–20] Possibly, the prevalence of circulating *C. trachomatis* serotypes that are more commonly associated with anorectal infection is relatively low in our study population.

One-third of women with oropharyngeal chlamydia or gonorrhea had the oropharynx as the only site of infection. The clinical relevance of this observation is directly related to the risk of transmission from oropharynx to penis with fellatio. Oropharyngeal coinfection has been reported for up to 18% of cases with urogenital chlamydia and 36% for urogenital gonorrhea.[15] Although fellatio as mode of transmission is well recognized for *N. gonorrhoeae*, no clear data are available about the transmission of *C. trachomatis* from oropharynx to penis. Sexual history reported by some patients suggests that this mode of transmission occurs for *C. trachomatis* as well.[21] In addition, oropharyngeal tests may indirectly increase detection of chlamydia and gonorrhea in case of false-negative endocervical tests. As such, we believe that oropharyngeal tests are useful for the detection of *C. trachomatis* and *N. gonorrhoeae* in female STD clinic visitors.

We observed an 11% increase in prevalence of chlamydia and gonorrhea by obtaining anatomical site-specific tests based on sexual history. Although this figure is not as dramatic as was reported for MSM in which the majority of infections may remain undiagnosed without taking oropharyngeal and anorectal samples, we consider that the observed increase in prevalence is substantial and relevant to warrant further evaluation.[9,12] Almost all cases of oropharyngeal and anorectal infection were asymptomatic and would thus have been missed when screening is done on the basis of reported pharyngitis or proctitis. Interestingly, a considerable proportion of women with isolated oropharyngeal or anorectal infection presented with symptoms of cervicitis only. Possibly, a number of these cases are related to false-negative endocervical tests, and oropharyngeal and anorectal tests may thus indirectly benefit women with undiagnosed endocervical infection. Furthermore, the positive predictive values of cervicitis, pharyngitis, and proctitis for *C. trachomatis* and *N. gonorrhoeae* infection are very low. Hence, if multiple anatomical site testing is performed, screening of asymptomatic women on basis of sexual history is superior to screening of symptomatic women.

We used a screening strategy based on sexual history instead of opportunistic screening of multiple anatomical sites regardless of exposure for several reasons. First, we think that the proportion of female STD clinic visitors that does not report fellatio or anal intercourse because of embarrassment is small. In addition, obtaining oropharyngeal and anorectal samples from women that deny fellatio and anorectal intercourse may be experienced as embarrassing and pose a considerable physical burden. Finally, we expect a relatively low positivity rate for anatomical sites for which no sexual contact is reported. However, studies are warranted that compare the approach of screening of anatomical sites based on sexual history with opportunistic screening of all anatomical sites. On the other hand, the sexual history-based approach may be even further refined by using specific risk factors or an algorithm as an entry point in the future.

This study has several limitations. First, because of the set-up and anonymous character of the database, a client can be included in the database with multiple visits related to different episodes. Second, the analyzed data were collected during routine clinical consultations. Information that is not included in the standard questionnaire was not captured systematically, for example the presence of pharyngitis was only recorded if a patient complained about sore throat. Finally, the reliability of reporting of sexual history is unknown and may result in undertesting: women may not report specific sexual behaviors because of embarrassment or for other reasons. As such, more studies are highly warranted to confirm our findings.

Altogether, our data indicate that screening of oropharynx and anorectum based on sexual history has a substantial contribution to STD prevalence in women and warrants further exploration. Oropharyngeal and anorectal tests may be included in STD screening programs at little extra cost, especially if swabs from different anatomical locations were combined in a single collection tube and analyzed simultaneously. However, cost-effectiveness studies are needed to confirm this approach.

In conclusion, inclusion of oropharyngeal and anorectal tests in the STD screening protocol for women increases the prevalence of chlamydia and gonorrhea. In that context, screening of anatomical sites based on sexual history is to be preferred over a symptom-based approach.

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