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Nucleic Acid Amplification Tests for Diagnosis of *Neisseria gonorrhoeae* Oropharyngeal Infections▽

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The optimal methods for the diagnosis of pharyngeal *Neisseria gonorrhoeae* infection are uncertain. The objective of this study was to define the performance of culture and nucleic acid amplification tests (NAATs) for the diagnosis of pharyngeal *N. gonorrhoeae*. In this cross-sectional study, males and females >15 years old who acknowledged performing fellatio or cunnilingus (in the previous 2 months) were recruited from three clinics (two human immunodeficiency virus clinics and one sexually transmitted diseases clinic) located in Birmingham, AL. The test performance of culture for *N. gonorrhoeae*, the Gen-Probe Aptima Combo 2 transcription-mediated amplification assay (TMA), the BD ProbeTec ET amplified DNA strand displacement assay (SDA), and the Roche Cobas Amplicor PCR was defined by using a rotating "gold standard" of any positive results by two or three of the three tests that excluded the test being evaluated. A total of 961 evaluable test sets were collected. On the basis of a rotating gold standard of positive results by two of three comparator tests, the sensitivity and the specificity were as follows: culture for *N. gonorrhoeae*, 50.0% and 99.4%, respectively; PCR, 80.3% and 73.0%, respectively; TMA, 83.6% and 98.6%, respectively; and SDA, 93.2% and 96.3%, respectively. On the basis of a rotating gold standard of positive results by three of three comparator tests, the sensitivity and specificity were as follows: culture for *N. gonorrhoeae*, 65.4% and 99.0%, respectively; PCR, 91.9% and 71.8%, respectively; TMA, 100% and 96.2%, respectively; and SDA, 97.1% and 94.2%, respectively. In conclusion, currently available NAATs are more sensitive than culture for the detection of pharyngeal gonorrhea in at-risk patients. PCR is substantially less specific than culture, TMA, or SDA and should not be used for the detection of pharyngeal gonorrhea.

In the latter part of the 1990s, testing for *Neisseria gonorrhoeae* genital infections was revolutionized by the introduction of nucleic acid amplification tests (NAATs), which achieve sensitivities greater than those of traditional culture methods and which also allow the use of simplified means of specimen collection. For testing of specimens from genital sites, these tests have been found to be preferred by patients (because specimens can be collected less invasively) and by clinicians (because of the ease of specimen collection and increased sensitivity) and permit expanded screening both in traditional clinical settings and at outreach sites where testing has not typically been performed. At present, however, there are few published data on the performance of NAATs commercially available in the United States for the diagnosis of *N. gonorrhoeae* infections at nongenital sites of exposure.

Recent data suggest that oral-genital sexual contact is relatively common and may be increasing among Americans, particularly adolescents and young adults (7, 15, 17, 18). The importance of the oropharynx as a potential site of infection is further emphasized by a recent population-based study in which over 75% of heterosexual males and females reported that they had previously had oral sex. Among some subgroups, such as men who have sex with men (MSM), oral sex is more common than rectal sex and may represent the only site of sexual exposure (14). Thus, oral sex is not uncommon, both among heterosexuals and among MSM, and oral-genital contact places persons at risk for the acquisition of pharyngeal gonococcal infection, which may be transmitted to others (11), and for complications, including disseminated gonococcal infection (1, 3, 22, 24).

The majority of pharyngeal gonococcal infections are asymptomatic, and, thus, without accurate risk assessment and sensitive diagnostic methods, many of these infections are not diagnosed or effectively treated, providing a reservoir of disease in the community (13, 16). Estimates of the prevalence of gonococcal pharyngeal infection vary substantially according to the population studied. By the use of culture, pharyngeal infection has been documented in 3% to 7% of heterosexual men, 5% to 20% of heterosexual women, and 10% to 25% of MSM with gonococcal infection (8). A more recent longitudinal cohort study of MSM which utilized NAAT-based testing found a pharyngeal gonorrhea prevalence of 5.5% and an incidence rate of 11.2 cases per 100 person-years (13). As a result of these and similar data, the Centers for Disease Control and Prevention currently recommends a test for pharyn-

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geal infection with *N. gonorrhoeae* in MSM who have acknowledged participation in receptive oral intercourse during the preceding year. Guidelines for pharyngeal screening of heterosexuals are currently lacking (23). No NAAT is cleared by the FDA for the detection of *N. gonorrhoeae* in pharyngeal specimens, greatly restricting the use of NAATs to meet the needs mentioned above. Expansion of peer-reviewed performance information would permit the manufacturers to assess the utility of seeking clearance and, pending FDA clearance, permit clinical laboratories and their clients to assess the wisdom of these laboratories conducting the necessary Clinical Laboratory Improvement Act verification studies to make the tests available.

The objective of this study was to define the performance for diagnosis of pharyngeal or rectal *N. gonorrhoeae* infection of culture and NAATs commercially available in the United States. In this report, we present the findings of the pharyngeal testing component of the study.

MATERIALS AND METHODS

Study procedures. From July 2003 until December 2006, at-risk patients at three participating Birmingham, AL, clinics were approached for study enrollment. The participants were recruited from the Jefferson County Department of Health Sexually Transmitted Diseases (JCDH STD) Clinic (males and females), a county hospital-based human immunodeficiency virus (HIV) clinic (males and females), and a university hospital-based HIV clinic (males only). At each site, the participants were eligible for enrollment if they were over age 15 years, had performed cunnilingus or fellatio within the 2 months prior to study enrollment, and were willing and able to sign written informed consent. They were ineligible if they had received antibiotics active against *N. gonorrhoeae* and/or *Chlamydia trachomatis* within 30 days prior to study enrollment. Following the provision of consent, each participant answered a brief survey and underwent the collection of four pharyngeal swab samples. The specific swabs used for specimen collection included the following: a cotton-tipped swab for inoculation onto gonorrhea culture medium, a Dacron swab for PCR (Cobas Amplicor), and swabs contained in the test kits for the Gen-Probe Aptima Combo 2 and the BD ProbeTec ET amplified DNA assays. Each specimen was collected from both tonsillar pillars and the posterior pharynx of the study participant. Following collection, the specimens were stored according to the manufacturers' instructions. From July 2003 to July 2005, specimens for PCR were placed in 2-SP transport medium; subsequently, following in-house validation studies demonstrating a 100% concordance between the results obtained with 2-SP and M4 media, the laboratory switched to M4 transport medium. Specimens for culture were directly inoculated onto GC-Lect agar and were incubated at 35°C in a CO_2 atmosphere within 30 min of collection. The swab order was rotated every 3 months throughout the study period. All specimens were transported to the University of Alabama STD Research Laboratory daily for testing. The tests performed included *N. gonorrhoeae* culture, the Gen-Probe Aptima Combo 2 transcription-mediated amplification assay (TMA; version 5.16; Gen-Probe Inc., San Diego, CA), the Roche Cobas Amplicor PCR (version 2.0; Roche Diagnostics Systems Inc., Pleasanton, CA), and the BD ProbeTec ET amplified DNA strand displacement assay (SDA; version 3.11B; Becton Dickinson and Co., Sparks, MD).

Patients recruited at the JCDH STD clinic underwent genital and rectal (if participants reported rectal exposure) testing on the day of enrollment according to the clinic's protocol. In addition, female participants who were returning to clinic for treatment for a previously collected positive gonococcal and/or chlamydial test or who reported contact with an individual with *N. gonorrhoeae* or *C. trachomatis* infection or nongonococcal urethritis were tested for rectal infection, irrespective of their exposure history. Testing of genital specimens was performed in the context of usual care by the use of gonococcal culture, the Gonostat methodology, or, later in the study, the Gen-Probe Aptima Combo 2 assay. Participants recruited from each HIV clinic may or may not have had genital testing on the day of enrollment, as genital testing was performed at their primary care provider's discretion. When genital testing did occur, an NAAT-based test was utilized.

Patients recruited from each HIV clinic were advised to contact study staff within 5 days of testing to check on the test results. Patients enrolled from the JCDH STD Clinic were advised to contact the health department to receive their test results, according to the health department routine. Patients with negative study-related test results were not contacted routinely, unless the participant specifically requested that he or she be notified. Regardless of the recruitment site, all patients with one or more positive tests were contacted by the study principal investigator in order to discuss their results. All patients with one or more positive NAAT results were informed that NAATs are not currently cleared by the FDA for use for the diagnosis of pharyngeal gonorrhea and were offered treatment at no cost at the site from which they were recruited. Treatment for pharyngeal gonorrhea included ceftriaxone at 125 mg intramuscularly in a single dose or ofloxacin at 400 mg orally in a single dose (2, 23). All study procedures were approved by the institutional review boards of the Centers for Disease Control and Prevention, the University of Alabama at Birmingham, the Cooper Green Hospital, and the Alabama Department of Public Health.

Laboratory methods. For *N. gonorrhoeae* culture, GC-Lect medium (for testing of oral specimens) was directly inoculated and incubated at 35°C in 5% CO_2 within 30 min of specimen collection, examined after overnight incubation, and, if the result was negative, examined daily for another 2 days. Typical colonies containing gram-negative diplococci and giving a positive oxidase reaction were presumptively identified as *N. gonorrhoeae* and were subcultured onto chocolate agar. The identity of the presumptive *N. gonorrhoeae* isolates was confirmed by the NET test (Remel) (5). Testing for *N. gonorrhoeae* was performed by PCR (Roche Cobas), TMA (Aptima Combo 2 assay), and SDA (BD Probetec). The procedures for the NAATs were performed according to the instructions in the package inserts. The BD ProbeTec SDA and Roche Cobas PCR tests were performed with internal inhibition controls. The Aptima Combo 2 TMA does not require an internal amplification control, since it has a target capture step prior to amplification. Retests following initial equivocal or indeterminate results were performed with the original specimens. For the Aptima Combo 2 TMA and the BD ProbeTec SDA, equivocal results normally represent inhibition, and in the case of an equivocal result, the test was repeated. If a second equivocal result was obtained, the final result was classified as unevaluable. For the Roche Cobas PCR, results that were in the gray zone were handled by processing an additional aliquot of the original specimen and then repeating the test in duplicate. The final result was classified as positive, negative, or unevaluable on the basis of the results of all three tests (initial and duplicate repeat tests).

Statistical analysis. All questionnaire data were directly scanned into a database by using TeleForm software (version 8.2; Cardiff, Vista, CA), and all laboratory results were entered into the database. Genital *N. gonorrhoeae* test results obtained through standard patient care were abstracted through medical record review. Oropharyngeal test sets were eligible for inclusion in this analysis if they were complete and if the results of all four tests were either positive or negative. Test sensitivity and specificity were calculated by using a rotating standard which compared each test under evaluation with a performance standard that classified subjects as infected if the results of two or more of the three remaining comparator tests were positive (12). A second standard was applied in which each test was compared to a performance standard that classified subjects as infected only if the results of all three of the remaining comparator tests were positive. The 95% confidence interval (CI) was calculated on the basis of an exact binomial distribution. All the statistical analyses were performed with SAS software (SAS OnlineDoc 9.1.3, 2002 to 2005; SAS Institute Inc., Cary, NC).

RESULTS

Study population. From July 2003 through February 2007, 1,676 individuals were eligible for enrollment in this study, conducted to evaluate the performance of NAATs for the diagnosis of oropharyngeal and rectal gonorrhea and chlamydia infection. Of these, 912 (54.4%) agreed to be enrolled and were also eligible for the oral testing component of the study (data for the study of rectal infections will be reported separately). The 912 eligible individuals contributed a total of 1,101 oropharyngeal test sets (some participants were tested on multiple occasions over the course of the study). Of these, 140 (12.7%) test sets were excluded, leaving 961 evaluable test sets from 812 individuals, 122 (15%) of whom contributed two or more sets. Among the 140 excluded test sets, 126 were excluded because one or more tests in the set contained a result that was neither positive nor negative, including 124 (98.4%) sets that were excluded due to unevaluable or inconclusive

TABLE 1. Study population characteristics

Characteristic	Male (n = 675, 70.2%)	Females (n = 286, 29.8%)	Total (n = 961, 100.0%)
Median (range) age (yr)	36 (16–72)	24 (16–49)	32 (16–72)
No. (%) of individuals of the following race[a]			
White	344 (51.6)	57 (20.0)	401 (42.2)
Black	316 (47.4)	224 (78.9)	540 (56.8)
Multirace or other	7 (1.1)	3 (1.1)	10 (1.1)
No. (%) of individuals seen at the following recruitment site			
County HIV clinic	95 (14.1)	32 (11.2)	127 (13.2)
University HIV clinic	317 (47.0)	NA[b]	317 (33.0)
STD clinic	263 (38.9)	254 (88.8)	517 (53.8)
Median (range) no. of partners in previous 2 mo	3 (0–120)	2 (0–101)	2 (0–120)
No. (%) of individuals with a partner of the following gender in the previous 2 mo[c]			
Female	182 (27.0)	11 (3.9)	193 (21.9)
Male	419 (62.1)	245 (85.7)	664 (75.5)
Both	12 (1.8)	11 (3.9)	23 (2.6)
No. of individuals with genital gonococcal infection/total no. tested (%)[d]	30/338 (8.9)	21/214 (9.8)	51/552 (9.2)

[a] Race was missing for eight males and two females.
[b] NA, not applicable.
[c] The gender of the partner in previous 2 months was missing for 19 females and 62 males.
[d] Oral test sets for 337 males and 72 females were not accompanied by genital testing.

PCR results and one set each due to uninterpretable TMA and SDA results. Fourteen sets were excluded due to incomplete collection of the set.

The study population (Table 1) differed substantially by gender in terms of age, racial group, and recruitment site. Five hundred fifty-two (57.4%) of the oropharyngeal test sets were collected concomitantly with (or within 1 month of) genital testing. Among the genital specimens contributed by females, 9.8% (21/214) were positive for *N. gonorrhoeae*, while 8.9% (30/338) of the male genital specimens were positive.

Test performance. Test sensitivity was calculated by using a rotating standard which compared each test under evaluation with a performance standard defined as positive results by any two of three comparator tests. A second standard was applied in which each test was compared to a performance standard defined as positive results by three of three comparator tests. On the basis of a rotating gold standard of positive results by two of three comparator tests, the sensitivity varied from 50.0% for culture to 83.6% and 93.2% for TMA and SDA, respectively. The specificity ranged from 96.3% to 99.4% for these tests; PCR, on the other hand, had a sensitivity of 80.3% and a specificity of 73.0% for the diagnosis of pharyngeal gonorrhea (Table 2). When the standard of positive results by three of three comparator tests was applied, performance ranged as follows: gonococcal culture, sensitivity of 65.4% and specificity of 99.0%; PCR, sensitivity of 91.9% and specificity of 71.8%; TMA, sensitivity of 100% and specific-

TABLE 2. Estimates of sensitivities and specificities of SDA, PCR, TMA, and culture for detection of *N. gonorrhoeae* by reference standard

Standard and test	No. of infected individuals	% Sensitivity (95% CI)	No. of observations	% Specificity (95% CI)
Infected if the results of any two of three comparator tests were positive; otherwise, uninfected				
SDA	59	93.2 (83.5–98.1)	902	96.3 (94.9–97.5)
PCR	66	80.3 (68.7–89.1)	895	73.0 (69.9–75.9)
TMA	67	83.6 (72.5–91.5)	894	98.6 (97.5–99.2)
Culture	76	50.0 (38.7–61.7)	885	99.4 (98.7–99.8)
Infected if the results of all three comparator tests were positive; otherwise, uninfected				
SDA	35	97.1 (85.1–99.9)	926	94.2 (92.5–95.6)
PCR	37	91.9 (78.1–98.3)	924	71.8 (68.7–74.6)
TMA	34	100 (89.7–100)	927	96.2 (94.8–97.4)
Culture	52	65.4 (50.9–78.0)	909	99.0 (98.1–99.6)

TABLE 3. Pharyngeal gonorrhea prevalence by gender, type of oral exposure, and test performed[a]

Type of test	No. (%) of individuals of the following gender engaging in the indicate types of sexual activity:					
	Male			Female		
	Fellatio only (n = 417)	Cunnilingus only (n = 178)	Both (n = 9)	Fellatio only (n = 243)	Cunnilingus only (n = 13)	Both (n = 8)
SDA	36 (8.6)	10 (5.6)	1 (11.1)	26 (10.7)	0 (0)	2 (25.0)
PCR	106 (25.4)	56 (31.5)	3 (33.3)	78 (32.1)	5 (38.5)	3 (37.5)
TMA	26 (6.2)	9 (5.1)	1 (11.1)	20 (8.2)	0 (0)	2 (25.0)
Culture	15 (3.6)	5 (2.8)	1 (11.1)	13 (5.4)	0 (0)	1 (12.5)
Positive result by culture or two or more NAATs	31 (7.4)	10 (5.6)	1 (11.1)	22 (9.1)	0 (0)	2 (25.0)

[a] Questionnaire data were missing for 53 male oral test sets and 6 female oral test sets.

ity of 96.2%; and SDA, sensitivity of 97.1% and specificity of 94.2% (Table 2).

***N. gonorrhoeae* prevalence by activity and test performed.** Fellatio was performed by 426 (63.1%) men and 251 (87.8%) women within the previous 2 months, while 187 (27.7%) men and 21 (7.3%) women reported performing cunnilingus during this time frame. About 3% of the women and 1.3% of the men reported participating in both activities. By using gonococcal culture, the prevalence of pharyngeal infection was 3.5% (21 infections) among the men and 5.3% (14 infections) among the women. The prevalences determined by using a gold standard of positive culture results or positive results by two or more NAATs were higher: 7.0% (42 infections) for men and 9.1% (24 infections) for women.

The prevalence varied by the type of activity (Table 3) reported and by the test performed. For instance, on the basis of the culture results, the prevalence of gonorrhea among the male participants was 3.6% among those who performed fellatio only, 2.8% among those who performed cunnilingus only, and 11.1% among those who performed both activities. Among the female participants, 5.4% of those who participated in fellatio only had gonorrhea on the basis of culture results, whereas none of those participating in cunnilingus only and 12.5% of those performing both activities had gonorrhea.

Changes in the prevalence of gonorrhea by pharyngeal testing. While not all participants underwent genital tract testing for *N. gonorrhoeae* at the time of study enrollment, genital test results were available for 552 (57%) of participant visits. In these evaluations, by the use of the two of three positive test comparator and/or positive gonococcal culture results to define the presence of pharyngeal infection and a positive gonorrhea test (i.e., gonococcal culture, Gonostat, or later in the study, the Gen-Probe Aptima Combo 2 TMA) obtained through standard clinical care to define genital infection, 82 (14.8%) participants had gonorrhea. Among the 82 participants with gonorrhea, 23 (28.0%) had a positive test result for both the genital and pharyngeal sites, 28 (34.1%) were infected at the genital site only, and, importantly, 31 (37.8%) were infected only at the pharyngeal site (Table 4). If pharyngeal gonococcal culture alone had been used to define the presence or the absence of infection in these patients, the prevalence of gonorrhea would have been substantially lower; one in five infections would have been missed (data not shown).

DISCUSSION

This study, conducted to evaluate the performance of currently available NAATs and culture for the detection of *N. gonorrhoeae* within the oropharynx, demonstrates that each of the three NAATs is substantially more sensitive than culture. On the basis of the standard of positive results by two of three comparator tests positive, the sensitivities ranged from 50.0% (95% CI, 38.7 to 61.7%) for gonococcal culture to 80.3% (95% CI, 68.7% to 89.1%) to 93.2% (95% CI, 83.5% to 98.1%) for the NAATs. By utilizing positive results by three of three comparator tests as the standard, the sensitivities ranged from 65.4% (95% CI, 50.9% to 78.0%) for culture to 91.9% (95% CI, 78.1% to 98.3%) to 100% (95% CI, 89.7% to 100%) for the NAATs. The sensitivity estimates among the three NAATs were similar, but the specificity of PCR was substantially worse than the specificities of the other NAATs. While the specificities of SDA and TMA were slightly lower than the specificity of culture, they were probably still within an acceptable range for many clinical situations. PCR, on the other hand, yielded specificities of 73.0% (95% CI, 69.9% to 75.9%) on the basis of the standard of positive results by two of three comparator tests and 71.8% (95% CI, 68.7% to 74.6%) on the basis of the standard of positive results by three of three comparator tests, respectively. These data lend support to the findings of a recently published study of the performance of NAATs with specimens from the oropharyngeal and rectal sites conducted with a large population of MSM. That study found that SDA and TMA were far superior to culture for the detection of gonococci from the oropharynx, and the investigators in that study terminated the performance of PCR analysis early in the study due to the test's poor specificity (78.9%) for the detec-

TABLE 4. Gonococcal infection by site

Site(s) positive	No. (%) of individuals
Genital[a] and oral[b] sites positive	23 (28.0)
Genital site only positive	28 (34.1)
Oral site only positive	31 (37.8)
Total genital or oral sites positive	82 (100.0)

[a] Genital infection was defined as a positive result by a standard-of-care genital test (i.e., gonococcal culture, Gonostat, or an NAAT-based test).

[b] Oral infection was defined as a positive culture result and/or positive results by two or more NAATs.

tion of *N. gonorrhoeae* (20). Other investigators have noted that the Roche PCR and the BD SDA for *N. gonorrhoeae* may detect oropharyngeal commensal bacteria such as *N. cinereae* and *N. subflava* (6, 19, 20, 21; Becton Dickinson and Company, BDProbeTec ET *Chlamydia trachomatis* and *Neisseria gonorrhoeae* amplified DNA assays, package insert, 2001; Cobas Amplicor CT/NG test for *Neisseria gonorrhoeae* package insert, Roche Molecular Systems, Inc., Pleasanton, CA, 1999; M. J. Tuohy, G. S. Hall, M. Katanik, J. S. Knapp, D. J. Farrell, and G. W. Procop, unpublished data). In addition to *N. gonorrhoeae*. While there are relatively few studies of the prevalence of pharyngeal *Neisseria* species, one study reported that *N. cinereae* and *N. subflava* are present in the oropharynges of approximately one-third of individuals colonized by *Neisseria* species (10). While the specificity of the BD SDA was acceptable in the current study, the poor specificity of PCR makes the use of this assay for the detection of pharyngeal gonorrhea problematic.

Our study also provides data which demonstrate the analytic challenges associated with the definition of "infection" in the absence of an agreed upon gold standard and their impact on estimates of test sensitivity or specificity. A guiding assumption for our study was that traditional culture methods perform poorly for the detection of gonococcal pharyngeal infections, an assumption borne out by our findings. By using positive results of any two of three comparator tests to define infection, culture detected only 50% of the infections, while when we applied the more rigorous (more specific, but less sensitive) standard requiring the results of all three comparator tests to agree, the sensitivity of culture increased, but only to 65%. Had we chosen a still less stringent definition of sensitivity, requiring a positive result by only one of the three comparator tests to define infection, the estimated sensitivity of culture would have been still lower, while the estimated specificity would have been both higher and more stringently defined. The marked differences between the sensitivity of culture and the sensitivities of the NAAT-based tests for the detection of pharyngeal gonococcal infection suggests that use of the standard of positive results by three of three comparator tests (which required culture to be positive in order to meet the definition of "infected") when an NAAT-based test was being evaluated resulted in an overestimation of sensitivity and an underestimation of specificity for TMA, PCR, and SDA. The specificity of PCR for the detection of *N. gonorrhoeae* at the oropharyngeal site was extremely low, possibly due to cross-reaction with commensal nongonococcal *Neisseria* species. As eluded to above, there are differences in opinion as to the optimal way to approach test performance analyses. We believe that in the absence of an agreed upon gold standard, understanding the bias introduced by configuring the data is important and should be influenced by the aims of the investigation. We believe that the evaluation of relatively large numbers of specimens in this study as well as the use of three comparator assays, applied in rotating fashion, represents an acceptable approach to test evaluation and provides confidence in the accuracy of our estimates from tests conducted with high-risk populations. Our study strengthens earlier studies because of the use of fewer different comparison tests and provides one of the first studies to compare the performance of culture and three widely used, commercially available assays.

Our study also provides new insights into the epidemiology of oropharyngeal gonococcal infection, suggesting that among at-risk populations the prevalence of infection may be substantially higher than was previously estimated (4), especially among heterosexual females. While the purpose of this study was not to determine the transmissibility of gonorrhea through fellatio compared to that through cunnilingus, we were surprised that the prevalence of oral gonorrhea was similar across activities for males. Current STD screening guidelines focus on the testing of MSM with specimens from the oropharyngeal site (23). These data should be confirmed by studies with other, female populations, as the oropharynx of heterosexual females who practice fellatio may represent an underappreciated reservoir of asymptomatic gonococcal infection, especially in populations with a high prevalence of *N. gonorrhoeae* infection.

It was interesting that patients were not concordant for infection at all sites (Table 4). For example, when oral infection was defined as a positive culture result and/or positive results by two or more NAATs and genital infection was defined as a positive result by a standard-of-care test, we identified 82 gonococcal infections at the genital and/or oral site. Among the 82 infections detected, 28 (34.1%) were at the genital site only, 31 (37.8%) were at the oral site only, and 23 (28.0%) were at both sites. Therefore, this study further emphasizes the importance of the oropharynx as a reservoir of *N. gonorrhoeae*, in that over a third of infections would not have been detected if testing had been restricted to the genital site. It also suggests that estimates of the population prevalence of gonorrhea determined solely on the basis of genitourinary testing may be substantially underestimated. Our data are consistent with previously published data demonstrating that among MSM tested by the use of specimens from all anatomical sites (rectum, urethra, oropharynx), 36.4% of gonococcal infections were present at the oral site only (9). These results reinforce the screening recommendations for MSM (23). Our data extend these observations to males practicing cunnilingus and females practicing fellatio as well.

In conclusion, currently available NAATs are more sensitive than culture for the detection of pharyngeal gonorrhea in at-risk patients. PCR is substantially less specific than culture, TMA, or SDA and should not be used for the detection of pharyngeal gonorrhea. SDA and TMA therefore represent important new tools in the STD control armamentarium, and FDA clearance for the use of these tests with specimens from the oral site should be pursued. In the interim, clinical laboratories should consider conducting the necessary Clinical Laboratory Improvement Act verification studies to make these tests available for the testing of at-risk clients.

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