

New Recommendations for Routine Gonorrhea and Chlamydia Screening

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Neisseria gonorrhoeae (GC) and *Chlamydia trachomatis* (CT) are the two most common bacterial causes of sexually transmitted diseases (STD) in the United States. CDC estimates there are approximately 19 million new cases of STDs in a given year in the United States (of which, nearly 2 million of these are caused by GC/CT). The cost to treat these infections and their complications is estimated to be more than \$8 billion per year (1). The gold standard assay for diagnosis of GC/CT has been culture from appropriate specimens. However, culture can be problematic if specimens are not handled properly and inoculated onto the appropriate media (GC) or into appropriate cell lines (CT) immediately following specimen collection. *Neisseria gonorrhoeae* is particularly susceptible to dehydration in the absence of appropriate transport media.

Laboratories that perform GC/CT screening *en masse* (e.g., public health and other laboratories that service STD clinics) often utilize an automated nucleic acid amplification test (NAAT). These tests have been shown to have excellent sensitivity and specificity, with a quick turnaround time of less than one day in many cases. The NAAT allows the laboratorian the ability to test for both GC and CT in the same specimen using species-specific probes, and eliminates the need for time-consuming and sometimes difficult culturing techniques. The most commonly used NAATs in clinical laboratories take advantage of polymerase chain reaction (PCR) technology (COBAS Roche Amplicor), strand-displacement (SDA) assays (BD ProbeTec), or transcription-mediated amplification (TMA) technology (Gen-Probe Aptima).

FDA-approved specimens for use in NAATs include endocervical swabs from women, urethral swabs from men, and urine from both men and women. These specimens provide excellent potential for detection of GC/CT using any of the methods listed above. Additionally, vaginal swab specimens are FDA approved for use in TMA tests. Schachter *et al.* recently reported that vaginal swabs were equal to or superior to endocervical swabs or urine for detection of GC/CT in women (2). Thus, vaginal swabs are now considered the preferred sample type for screening (2, 3, 4). Recently, extra-genital sites (rectal, oropharyngeal) have been identified as potential sources for the detection of GC/CT. These sites have been useful in the diagnosis of GC/CT infection in patients who engage in high risk sexual practices, such as men who have sex with men (MSM) or sexually active young heterosexuals who engage in unprotected anal or oral sex. In an excellent review by Renault *et al.*, the sensitivity of NAATs using extra-genital specimens was at least as sensitive as culture for GC/CT (5). In patients with suspected rectal GC infection for whom rectal swabs were collected, TMA was considered the most sensitive test (100%), followed by SDA (78%), and PCR (54%) when compared to culture. When pharyngeal swabs were considered, the sensitivity of testing was again highest using TMA (95%), followed by SDA (75%), and PCR (66%). Where rectal CT infection was considered, the sensitivities for TMA, PCR and SDA were 100%, 92%, and 77%, respectively. In all cases, the specificity of extra-genital sites for NAATs was shown to approach 100%.

Rectal and pharyngeal infection among high risk populations remains a public health concern. The CDC currently recommends at least yearly screening for GC/CT for MSM since non-urethral infections are often asymptomatic and can be present in the absence of urethral infection (6). Annual screening for pharyngeal GC is also recommended for these individuals. In situations where a patient may have multiple sex partners or may participate in sex acts involving illicit drug use, CDC also recommends routine screening at 3 to 6 month intervals. Highlighting the importance of this recommendation, Kent *et al.* surveyed two STD clinics in San Francisco, CA with high MSM populations and found that 53% of CT and 64% of GC infections occurred at non-urethral sites (6). These infections would likely have gone undetected in the absence of routine extra-genital screening in this population.

Although the NAATs show an improved sensitivity for the detection of GC/CT infection, one drawback in using this methodology is the lack of positive cultures for additional testing. Of note is the inability to perform antimicrobial susceptibility testing on strains of *Neisseria gonorrhoeae*. Antibiotic resistance mechanisms are increasing among GC isolates, specifically to penicillin, tetracycline and ciprofloxacin. Due to this emerging resistance, the current CDC recommendation is that only cephalosporins be considered for the treatment of gonorrhea in the United States (7). For uncomplicated urogenital, anorectal, or pharyngeal GC, CDC recommends a single intramuscular dose of ceftriaxone (125 mg). In cases of suspected or diagnosed co-infection with CT, addition of a single dose of oral azithromycin (1 g) or a 7 day course of doxycycline (100 mg, twice daily) is recommended (7).

Culture has historically been considered the only forensic standard for the diagnosis of GC/CT infection in cases of suspected sexual abuse or assault. However, NAATs have now been seen as a reliable alternative for testing in these circumstances (8). A recent report from the Association of Public Health Laboratories in consultation with the CDC reported that NAATs were superior to culture for the detection of CT in cases of adult

rape or sexual abuse in adults and children (9). It is however still recommended that confirmatory testing using a different NAAT be considered when positive NAAT results for GC occur in either adults or children. Black *et al.* showed that urine specimens tested by NAATs provided a clear advantage over culture in sensitivity and was less invasive than swabs (8). The authors also pointed out that urine specimens, as opposed to swabs, also reduced patient trauma and discomfort, which is especially important with children being evaluated for sexual abuse. To date, these recommendations have yet to be widely accepted by courts of law.

Currently extra-genital site specimens are not FDA approved for use in commercially available NAATs. Laboratories that consider adopting these specimens for testing must verify and validate that the assay performs with the highest levels of sensitivity, specificity, accuracy and precision, as compared to previously verified testing. These parameters are currently being evaluated by the NPHL for both throat and rectal specimens. Additional validation testing is being considered for vaginal and eye specimens in the future. Culture will still be available in the laboratory for unusual specimens or in cases where an organism is needed for additional testing.

References

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