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A New Gold Standard for the Detection of *Chlamydia trachomatis*?

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Cell-culture techniques have long been considered the "gold standard" for the detection of *Chlamydia trachomatis*. The major advantage of cell-culture isolation is the specificity, which approaches 100%; however, even in experienced laboratories, its sensitivity is only 70–80%.[1–3] Its primary use has been in detecting symptomatic carriers in low-prevalence populations. Nonculture objective methods, such as enzyme immunoassay, DNA probe, polymerase chain reaction (PCR), and ligase chain reaction (LCR), have been used primarily in symptomatic or high-risk, high-prevalence asymptomatic populations (Table 1).

NEW GOLD STANDARD?

Lee et al. have proposed that the gold standard for *C. trachomatis* be redefined as all culture-positive as well as culture-negative LCR-positive individuals.[4] In a study of 1,935 women in which the first-voided urine specimens were compared to endocervical swabs using an LCR-based assay versus cell tissue culture techniques, the LCR assay showed a detection rate for infected women almost 30% greater than that of the endocervical swab cultures. The overall resolved sensitivity of LCR on first-voided specimen was 93.8%, compared with a sensitivity of only 65.0% for cultures of endocervical swab samples. The problem with urine tests is that prior culture studies have shown that 5–30% of infected women have only urethral colonization.[3] Only 50–60% of infected women have both endocervical and urethral infection.

In a subsequent study, Schachter et al. compared first-catch urine LCR test with cell culture isolations from the cervix and urethra. Compared with the cervical cultures, LCR was 88.2% sensitive and 100% specific. Adding urethral culture increased the tissue culture sensitivity from 67.1% to 74% and reduced LCR sensitivity to 85.9%.[5] The observed increase in sensitivity does not appear to be associated with a reciprocal loss of specificity. Tests of copies of genomic DNA of commonly isolated bacteria, protozoans, etc., in the urogenital tract were negative in all cases studied.[5–7]

Hadgu has focused a problem which will delay a final decision as to the new gold standard.[8] The discrepant analysis, which is used to provide estimates of sensitivity and specificity in the presence of an imperfect gold standard that has been applied to estimate the sensitivity and specificity of DNA-amplification tests for *C. trachomatis*, is usually biased.

PCR VERSUS LCR IN WOMEN BEING TESTED

Polymerase chain reaction tests are both sensitive and specific in detecting chlamydial infections in men; PCR may be slightly more sensitive than LCR assay in diagnosing *C. trachomatis* infection in men in a test of first-void urine. The problem with PCR is that endocervical specimens contain inhibitors that appear to reduce the sensitivity.[9–10] This susceptibility of PCR tests to inhibitive factors in cervical specimens can be significantly reduced by pretreatment procedures, including heating treatment or the use of 2SP transport medium. A 10-fold dilution of the clinical specimen followed by heating treatment further prevents inhibition of the PCR tests.

The problem of inhibitory factors in cervical samples and the inability to obtain screening specimens without using a speculum tend to sustain the

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TABLE 1. Non-culture tests for the detection of *Chlamydia trachomatis*

Test	Principle	Use
Direct fluorescent antibody	Utilizes antibodies directed against either the genus-specific lipopolysaccharide or the species-specific major outer-membrane proteins.	Advocated for small-volume testing where quality of the specimen is an issue.
Enzyme immunoassay	Detects chlamydia lipopolysaccharide with primarily polyclonal antibody that has been linked with an enzyme.	Best used in high-prevalence populations (owing to low sensitivity).
Nucleic acid hybridization (DNA probe)	Utilizes an acridinium ester-labeled single-stranded DNA probe that is complimentary to the RRNA of *Chlamydia trachomatis.*	
Amplification procedures (-polymerase chain reaction, -ligase chain reaction)	Amplifies a target DNA sequence via the designated enzyme. One molecule of target DNA can potentially be amplified one billion times.	Highest sensitivity

concept that LCR will become the methodology of choice for the discipline of obstetrics and gynecology. A new gold standard in terms of sensitivity and specificity appears in evolution and, when established, may be challenged by even new technologies. Obstetricians and gynecologists need to conceptually prepare for change. Beyond the choice of a new gold standard will be the issue of what, urine alone or endocervical and urine specimens combined, will be required for the gold standard test in women.

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