Detection of *Chlamydia trachomatis* Endocervical Infections by Ligase Chain Reaction versus ACCESS Chlamydia Antigen Assay

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Ligase chain reaction (LCR) was compared with ACCESS immunoassay for detection of chlamydial infections in females. Despite efforts to improve ACCESS performance by evaluation of specimens that were in the test performance “grey zone,” LCR remained more sensitive and was less expensive to perform. ACCESS had a sensitivity of 83.9%, a specificity of 99.7%, a positive predictive value of 96.3%, and a negative predictive value of 98.5%.

We compared ACCESS immunoassay (Beckman/Sanofi Diagnostics, Brea, Calif.) with ligase chain reaction using the Abbott LCx System (Abbott Laboratories, Abbott Park, Ill.) to diagnose *Chlamydia trachomatis* infections in women, and assessed the relative cost of each procedure. Three hundred fifty-six women presenting to the University of Alabama Hospital emergency department between July 1997 and April 1998 suspected of having chlamydial endocervical infections were studied with the approval of the university’s Institutional Review Board. Cervical swab specimens were collected for ACCESS and LCx assays, placed into transport systems, and stored at 4°C for ≤96 h prior to assay. The order of swab collection was randomized to prevent sampling bias, and each assay was performed independently by different personnel.

LCx was performed as previously described (5). The ACCESS immunoassay uses a monoclonal antibody coupled to paramagnetic particles to detect chlamydial lipopolysaccharide antigens by chemiluminescent enzyme immunoassay with the Beckman ACCESS analyzer. The presence or absence of chlamydial lipopolysaccharide antigen was determined by comparing the relative light unit (RLU) signal to a 20,000 RLU cutoff. The manufacturer’s recommended procedure was modified in an attempt to increase test sensitivity through careful evaluation of specimens whose results were in the assay’s performance “grey zone” by lowering the cutoff for a positive signal and retesting specimens with signals greater than or equal to 20,000 RLU. If specimens still tested positive, a blocking assay was performed with affinity-purified, equine antichlamydia antibodies that compete for specific epitopes on the extracted antigen, preventing formation of a complex with the monoclonal antibody. Suppression greater than or equal to 50% was considered positive. Specimens that produced discrepant results were tested blindly with a second LCx assay directed against the major outer membrane protein (MOMP) gene. A test was considered to be truly positive when a specimen tested positive by both LCx and ACCESS, or by LCx confirmed by a second LCx for the MOMP, if the initial testing result was discordant. This expanded definition of the “gold standard” for a positive test has been recommended in view of the enhanced sensitivity of DNA amplification tests over culture and nonamplified nonculture assays (1).

Thirty-one of 356 specimens tested positive after resolution, giving a prevalence of 8.7% (Table 1). One specimen initially reactive by ACCESS showed 57% suppression in the blocking assay. However, both the LCx and alternate-target LCx were negative, suggesting this was a false-positive reaction. Using confirmed positive results by LCx as a reference, ACCESS had a sensitivity of 83.9%, a specificity of 99.7%, a positive predictive value of 96.3%, and a negative predictive value of 98.5%. Using the manufacturer’s definition of a positive test, ACCESS would have correctly identified 25 of 31 samples testing positive, yielding a sensitivity of 80.6%. Thus, despite modifying the criteria for a positive test, ACCESS failed to match the detection rate of LCx.

In our laboratory, LCx not only demonstrated superior diagnostic sensitivity but also provided laboratory cost savings of approximately $4,950 yearly, based on $2.25 savings for each test performed. LCx also has a substantially higher Medicaid reimbursement rate than antigen detection assays (Table 2).

Despite the use of grey zone testing, and similar to other studies (1–7), LCx provided greater sensitivity for *C. trachomatis* detection than did ACCESS. To our knowledge, this is the first published evaluation of ACCESS for detecting chlamydial infections of the endocervix in comparison to nucleic acid amplification. Similarly, we are not aware of other studies that have compared the performance of ACCESS to other enzyme immunoassays and are therefore unable to comment further on its utility in relation to other commonly used nonamplified antigen detection products.

The extremely high specificity and positive predictive values of nucleic acid amplification assays make them realistic possibilities for many hospital-based or independent diagnostic laboratories (1). The institutional costs of implementing a specific type of procedure in a diagnostic laboratory and its acceptance and utilization by clinicians depend on many factors, some of which are specific to individual institutions, while others are more general. These factors include existing laboratory staffing, local labor costs, space, complexity of testing, controls required, instrumentation, test volume, realistic turnaround time, and work flow. Whether a test will be used primarily for
screening asymptomatic persons or for testing individual patients for diagnostic purposes impacts costs and the possibility of running tests in larger batches in order to reduce individual costs per test. The type of patient population served and type of specimen required can also impact the overall expense of an institution offering a specific procedure and thus influence the choice of tests used in the diagnostic laboratory.

LCx possesses numerous advantages over culture and nonamplification tests, including the ability to use voided urine as a diagnostic specimen, making it particularly amenable for screening asymptomatic persons (2, 6). In addition, the possibility of using a single, noninvasive diagnostic specimen such as urine for the detection of both Neisseria gonorrhoeae and C. trachomatis is also attractive for clinicians. Therefore, the value of instituting such potentially time-saving techniques which could permit more efficient patient management should be considered when a laboratory chooses diagnostic tests. Finally, utilization of a more sensitive nucleic amplification test for detecting chlamydial infections can potentially result in even greater savings when the costs of treating complications such as pelvic inflammatory disease in women whose infections were missed by other tests are considered (2). Based on these observations and data from the present study, we chose to implement the LCx for the detection of chlamydial infections in our emergency department and to offer clinicians the choice of submitting either urine or endocervical swabs for testing.

Abbott Laboratories, Diagnostics Division, provided reagents for the LCx assays.

Timothy Zurow of Abbott Laboratories performed the second LCx assay directed against the MOMP, and its ACCESS result was considered a false-positive result.

### REFERENCES


