Evaluation of the leukocyte esterase test (LET) as pre-screening test to reduce costs for national population-based Chlamydia trachomatis screening programs
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Published in:
Journal of Adolescent Health

DOI:
10.1016/j.jadohealth.2005.11.004

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2006

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
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To the Editor:

With great interest, we read the article by Blake and colleagues on the re-evaluation and potential re-appreciation of the Leukocyte Esterase Test (LET) as an initial screening test to be followed by nucleic acid amplification testing (NAAT) confirmation [1]. We too have recently evaluated the inexpensive LET as compared with commercial polymerase chain reaction (PCR) detection of Chlamydia trachomatis to prescreen urine samples obtained from an asymptomatic population. Below we summarize our results and propose evaluation and implementation tools based on the study of Blake et al [1] and our own results.

From the previously described PILOT study [2], which assessed the presence of C. trachomatis DNA by PCR (Roche Diagnostic System, Basel, Switzerland) in 8383 randomly selected women and men (aged 15–29 years) by using a home-sampling urine kit, we performed the LET as described by the manufacturer (Roche) simultaneously in 2100 of those subjects. In addition, the effect of longer LET test incubation (two vs. five minutes) was assessed to potentially identify more C. trachomatis DNA-positive patients. Finally, the effect of time from urine sampling until LET testing was determined.

By PCR, 55 subjects (2.6%) were identified as C. trachomatis DNA positive (all true positives as assessed by C. trachomatis serovar determination [3]). Using the LET, we identified 53% of the C. trachomatis DNA-positive subjects, whereas extended LET incubation identified 64%. As compared with two-minute incubation, 16% additional LET positives were identified after five-minute incubation (41% had identical LET values for two- and five-minute incubation and 57% had increased LET values after five-minute incubation). From the C. trachomatis DNA-negative subjects, two-thirds were LET negative (five-minute incubation). The time between urine sampling (home obtained) and LET testing (one to seven days) did not influence the identification of the number of C. trachomatis DNA-positive subjects.

The 36% C. trachomatis DNA-positive subjects missed using the above-described approach would be unacceptably high if the test was used for sexually transmitted infection (STI) diagnostic purposes. However, almost 90% of the C. trachomatis infections are asymptomatic, and these people will not seek medical attention and thus will not be treated in most cases anyhow. The question then arises whether using an inexpensive test with, however, a lower sensitivity as compared with NAAT, would result in health gains in terms of C. trachomatis-positive cases cured and complications averted that outweigh the screening costs. To answer this question, further studies are needed, which have to address the following:

- Cut-off value of LET (use trace [1]) and an extended incubation period to five minutes.
- Include a cost-effectiveness analysis comparing both LET and NAAT: retesting after prescreening by LET would reduce the number of expensive PCR tests by two-thirds (associated costs: EUR 25 for a PCR assay vs. EUR .40 for a LET).
- In addition, reduced costs associated with technician time and disposables will further significantly decrease total screening costs if LET is used as a prescreening test.
- Evaluate the use of both LET and nitrites, an approach forwarded in a recent meta-analysis of the urine dipstick test [4].
- The effect of preselection of the asymptomatic screening population based on recently described selection variables obtained in an over-10,000-person screening study [5].
Partner tracing efficiency versus screening only one gender: in most cases women have been suggested in single-gender screening approaches.

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do:10.1016/j.jadohealth.2005.11.004

The Authors reply:

We read Dr. Morré and colleagues’ letter with interest and appreciate their suggestion to increase the incubation period of the leukocyte esterase test (LET) to five minutes [1]. Now that home urine collection and population screening are a realistic possibility, it is encouraging to know that the time between urine sampling (home obtained) and LET testing did not influence the identification of C. trachomatis DNA-positive persons.

As we had previously commented [2] and Morré et al also indicate [1], the LET appears to miss a substantial proportion of C. trachomatis infections that are detected by a nucleic acid amplification test (NAAT). As they point out, the next question becomes, “Are the increased costs associated with the more sensitive test outweighed by the costs averted via detecting more infections?” We have been interested in the same question and have performed a cost-effectiveness analysis addressing this issue in a population of males, aged 14 to 18 years, in detention centers [3]. We found that it is not only cost-effective, but also cost-saving to screen all asymptomatic males in detention with a NAAT rather than selectively screening only the LET-positive males. This finding may be age and population dependent, however, and more studies are needed to confirm these conclusions in other groups, such as can be found in national screening programs.

Our screening strategy in detention not only provides the opportunity to treat current and recent past partners, but also may avert infection in future partners, who will not be exposed to the index male’s infection [3]. As a result, the additional cost of universal NAAT screening is outweighed by the cost savings associated with averting additional cases of pelvic inflammatory disease in female partners. Future cost-effectiveness studies are required to answer these important questions of how to best manage population-based screening programs for Chlamydia trachomatis infections.

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