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LS SALIMONU

SubDepartment of Immunology
Department of Chemical Pathology
University College Hospital,
Ibadan, Nigeria

Detection of *Chlamydia trachomatis* by enzyme immunoassay, immunofluorescence, and cell culture

Mumtaz *et al*¹ presented their evaluation of a commercial enzyme immunoassay (Abbott Laboratories) for detecting *Chlamydia trachomatis* in urethral and cervical specimens. The hospital and laboratory in which the work was performed has a long and well established research interest in *C trachomatis*. We present our experience with this enzyme immunoassay in a district general hospital that does not have such an established interest but wishes to provide a rapid and reliable service for the diagnosis of *C trachomatis* infection. We also simultaneously tested many of our patients using a third technique.

We evaluated 83 cervical specimens by enzyme immunoassay and a McCoy cell culture technique that was essentially similar to that described by Mumtaz *et al*¹ except that cell monolayers were stained with Giemsa. Cell cultures were not passaged. Specimens were taken from women on their first visit to the clinic of genito-urinary medicine, irrespective of their reason for attendance. Fifty five of these patients were also tested by direct immunofluorescence using a fluorescein labelled genus specific mono-

clonal antibody (Boots-Celltech Diagnostics). Specimens were considered to be positive if 10 or more fluorescing elementary bodies were seen. In each case the swab for enzyme immunoassay was taken before the swab for cell culture. If immunofluorescence was being performed the swab for culture was used to prepare a slide before it was placed in transport medium.

Comparison of cell culture, enzyme immunoassay, and immunofluorescence for detecting *C trachomatis* in cervical samples

Enzyme immunoassay	Cell culture	
	Positive	Negative
Positive	17*	3†
Negative	3‡	60§

* 11 tested by immunofluorescence: 10 positive; † Two tested by immunofluorescence: two positive; ‡ One tested by immunofluorescence: one positive; § 41 tested by immunofluorescence: 41 negative.

The Table shows the results. *C trachomatis* was isolated from 20 (24%) samples. Seventeen of these were positive by enzyme immunoassay. Of the three samples negative by enzyme immunoassay, one was positive by immunofluorescence. Two of the three cases that were negative by cell culture but positive by enzyme immunoassay were tested by immunofluorescence, and both were positive. None of the three patients whose samples were negative by cell culture had been treated with antibiotics in the few months before sampling.

Although the number of specimens evaluated was small, our results were similar to those of previous studies.¹⁻⁴ In addition, the results obtained indicate that specimens positive by enzyme immunoassay but negative by cell culture are not necessarily false positives but may represent the loss of viability of *C trachomatis* during transport. Our findings also raise some doubt about the use of cell culture as the "gold standard" and the value of defining a "specificity" (the number of healthy subjects with a negative test result divided by the total number of healthy subjects)⁵ for antigen detection assays.

If the enzyme immunoassay test is compared only with cell culture its specificity in our evaluation was 95% (60/63). Two of the three discrepant results were positive by immunofluorescence, and the third was not tested by this technique. If these results are taken to indicate that these two specimens were positive (and the third specimen dis-

regarded) the specificity of enzyme immunoassay may be considered to be 100% (60/60) in our small series. Similarly, the sensitivity of the enzyme immunoassay improves from 85% (17/20) to 86% (19/22) compared with a sensitivity for cell culture of 91% (20/22). Therefore, sensitivity and specificity figures must be interpreted with caution when the reference test is known to have a sensitivity of less than 100%.

In conclusion, although under ideal conditions cell culture may be more sensitive than enzyme immunoassay, in routine diagnostic use this is probably balanced by the failure to isolate *C trachomatis* from several infected patients. The use of such an enzyme immunoassay has resulted in a considerable improvement in our service, as we no longer encounter the problems of maintaining a ceiling of required sensitivity for the reliable isolation of *C trachomatis*.

P MORGAN-CAPNER

P HUDSON

J A CANSFIELD

A SAEED

Department of Virology,

Preston Infirmary,

Preston PR1 6PE

* Department of Genito-Urinary Medicine,

Royal Preston Hospital,

Preston PR2 4HT

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Comparison of methods for detecting *Chlamydia trachomatis*

Dr Ridgway and others reply as follows: Morgan-Capner *et al* raise the possibility that apparent false positive results with the new chlamydial antigen detection method may reflect deficiencies in the cell culture

Table Comparison of Enzyme immunoassay, immunofluorescence, and cell culture for specimens from 66 patients (31 men, 35 women)

Enzyme immunoassay	Immunofluorescence	Cell Culture	Total*
-	-	-	51 (27)
+	+	+	5 (3)
+	+	-	9 (4)
-	+	+	1 (1)

*Figures in parentheses represent women only.

technique. This is almost certainly the case. Towards the end of our reported study we noticed a decrease in the sensitivity of our cell culture technique. The study was therefore extended, and discrepant results between cell culture and enzyme immunoassay were re-examined using a direct immunofluorescence technique (Micro Trak Syva). Overall, 277 specimens were examined by cell cultures and enzyme immunoassay, comprising 158 cervical specimens and 119 male urethral specimens. Sensitivity and specificity for enzyme immunoassay were 81.25% and 95.2% for cervical specimens, respectively, and 95.3% and 97.5% for urethral specimens, respectively.

There were 22 discordant results: 13 were culture negative and enzyme immunoassay positive and nine culture positive and enzyme immunoassay negative. Of these, 10 specimens (nine enzyme immunoassay positive and culture negative) were available for immunofluorescence testing. In addition, five specimens positive by enzyme immunoassay and culture and 51 randomly selected specimens negative by both methods were retested using immunofluorescence.

Immunofluorescence testing was carried out by placing an aliquot of the remaining enzyme immunoassay specimen (held for a variable period at -70°C) on a 10 mm well of a teflon coated slide. After fixation in cold acetone for 30 minutes the preparation was stained according to the manufacturer's instructions (Micro Trak Syva).

The Table shows the results. All nine culture negative and enzyme immunoassay positive specimens and the single enzyme immunoassay negative culture positive specimen were immunofluorescence positive. Immunofluorescence results on the 56 non-discordant specimens agreed with the cell culture and enzyme immunoassay findings. Thus when checked against immunofluorescence only one enzyme immunoassay result was truly false (negative). Incorporating these results into our calculations the sensitivity and specificity improve from 81.25% to 83.3% and 95.2% to

98.4%, respectively, for cervical specimens and from 91.9% to 92.9% and 91.5% to 97.4% for urethral specimens, respectively.

Taylor-Robinson, Hawkins, and Thomas,¹ cautioned against misinterpreting immunofluorescence test results that produce apparent high identification rates for *C trachomatis*. As enzyme immunoassay methods are not subjective this should be less of a problem with these techniques. Sensitivity and specificity with enzyme immunoassay will, however, reflect the optical density cut off setting, and some results will fall in the "retest range."

It is well accepted that cell culture, even in the best hands, is not 100% successful; but until more extensive experience is obtained with the new methods, epidemiological and treatment studies based solely on antigen detection techniques must be interpreted with caution.

Reference

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GL RIDGWAY

JD ORIEL

G MUMTAZ

B MELLARS

Department of Clinical Microbiology,
University College Hospital,
Grafton Way,
London WC1E 6AV

Influence of laboratory sensitivity reporting on antibiotic prescribing preferences of general practitioners in the Leeds area

A survey made over two periods of time was used to determine the effect of a limited antibiotic reporting policy on the prescribing habits of general practitioners in the Leeds area.

During the autumn of 1983 a policy of limited antibiotic reporting was adopted by the senior medical staff of the microbiology department of Leeds General Infirmary. This policy called for the laboratory to suggest the use of single agents that were considered to be less toxic, less expensive, or less likely to cause bacterial antibiotic resistance, for the treatment of inpatient, outpatient, and general practitioner patients, from whom a significant isolate had been obtained. A laboratory report for a patient with uncomplicated urinary tract infection would normally indicate the susceptibility of the isolate to trimethoprim, sulphonamides, and nitrofurantoin. Alternative antibiotics would be reported if indicated by the clinical condition of the patient. For this scheme to be effective full clinical details of the patient are required by the laboratory. Completed laboratory reports therefore carried comments indicating to the clinician the importance of clearly stating the patient's condition, the duration of illness, length of pregnancy if applicable, and any recent or current treatment with antibiotics, whether or not prescribed for urinary tract infection. Antibiotics prescribed for other conditions may be excreted in adequate quantities in the urine to preclude the isolation of a clinically important organism, although urinary tract infection itself may persist.

Hospital clinicians normally respond to advice given by the laboratory on the use of antibiotics; there is, however, some doubt about the influence of the laboratory on the prescribing patterns of general practitioners. To determine the influence of the limited antibiotic reporting policy on the prescribing habits of general practitioners a survey was carried out by the laboratory shortly after the policy was introduced and repeated twelve months later. The survey entailed asking general practitioners for their preferred antibiotic for use in the treatment of urinary tract infection; a laboratory method monitored incoming urines for content and subsequent identification of antimicrobial substances.¹

In the winter of 1983-4 a questionnaire was issued to 149 general practitioners within the western Leeds area to whom the Infirmary laboratory is responsible for the handling of specimens. Twelve months later the questionnaire was reissued and the responses compared. The questionnaire described six circumstances in which a general practitioner might find him or herself when dealing with a patient presenting with symptoms of urinary tract infection. Each question asked the general practitioner to indicate his choice of antibiotic. The content