

Poor Performance of a Novel Serological Test for Diagnosis of Pulmonary Tuberculosis in Bangui, Central African Republic

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We assessed the performance of a serological test for tuberculosis (SDHO Laboratories Inc., Canada) in our setting. Among 68 of 99 suspected pulmonary tuberculosis patients who were scored as having tuberculosis on the basis of *Mycobacterium tuberculosis*-positive culture, the sensitivity of the serological test was lower than that of sputum smear microscopic examination (20.6% versus 80.9%, respectively; $P < 0.000001$).

Tuberculosis (TB) remains a major health problem, with an estimated 8 million new cases and 2 million deaths due to this disease every year worldwide (4). Microscopic examination of sputum smears is still the only rapid, technically simple, and inexpensive test available for the routine diagnosis of TB in most developing countries. However, its sensitivity for pulmonary tuberculosis (PTB), even in good centers, is only about 60 to 70% with reference to sputum culture. Various antibody-based serological tests have been developed. Unfortunately, most do not perform sufficiently well to be used as routine field diagnostic tests (6, 9, 11, 12). Here, we assessed the diagnostic performance of the SDHO MTB test (SDHO Laboratories Inc., Canada), a novel and commercially available serological test for the detection of PTB, in the Central African Republic, which is a setting with high prevalences of both TB (13) and human immunodeficiency virus (HIV) infection (1, 7).

Study participants were recruited from the Department of Medicine at Bangui Community Hospital and from the Chest Clinic at National Teaching Hospital in Bangui, Central African Republic, between 12 July and 1 September 2004. Eligible participants were suspected PTB cases, defined as patients who had a history of cough lasting ≥ 3 weeks and who were identified by a physician as needing an evaluation for TB. Giving of informed consent, age of ≥ 18 years, and either sex were considered inclusion criteria for the study. All consecutive suspected PTB patients who fulfilled the inclusion criteria were enrolled and underwent an evaluation that is considered routine for suspected PTB in the Central African Republic. This consisted of providing three sputum specimens for acid-fast bacillus smearing within 48 h of enrollment. In addition, these same sputum specimens and blood samples were processed for mycobacterial culture (3, 5). Blood samples were also used for HIV testing as described elsewhere (8).

The SDHO MTB test (SDHO Laboratories Inc., Canada) utilizes the principle of immunochromatography and is a unique two-site immunoassay on a membrane. As the test sample flows

through the membrane assembly of the device, a colored recombinant TB antigen-colloidal gold conjugate complexes with anti-TB antibodies in the sample. This complex moves through the membrane to the test region, where it is immobilized by the recombinant TB antigen coating of the membrane, leading to formation of a colored band which confirms a positive test result. The absence of this colored band in the test region indicates a negative test result. The unreacted conjugate and unbound complex, if any, move further on the membrane along with rabbit immunoglobulin G (IgG) in the colloidal gold conjugate and are subsequently immobilized by goat anti-rabbit antibodies on the membrane at the control region, forming a pink band. This control band serves to validate the test results. In our laboratory, the test was performed with 50 microliters of blood serum specimens as soon as possible on the day of collection. The results were interpreted after 15 min of migration, according to the instructions of the manufacturer.

Patients were confirmed as having PTB disease on the basis of positive sputum and/or blood culture for *Mycobacterium tuberculosis*. Sensitivity, specificity, and positive and negative predictive values were assessed for microscopic examination and for the serological test. Chi-square and Yates corrected P values were used for comparisons of performance between these two methods.

A total of 99 suspected PTB patients were included for evaluation during the study period. The median age was 31 years (range, 18 to 72 years), with 53 men and 46 women. Among 98 patients who accepted the HIV serology test, 55 (56.1%) were HIV positive. *M. tuberculosis* was isolated from 31 (56.4%) of the HIV-positive patients and from 37 (86.0%) of the HIV-negative patients ($P < 0.002$). The patient who refused HIV testing was culture negative for *M. tuberculosis*. The sensitivity of sputum smear examination was much lower among HIV-positive PTB patients (21 of 31; 67.7%) than among HIV-negative PTB patients (34 of 37; 91.9%) ($P < 0.01$). A similar tendency was observed for the SDHO MTB test; the sensitivity was 16.1% (5 of 31) among HIV-positive PTB patients and 32.4% (12 of 37) among HIV-negative PTB patients. However, this difference was not statistically significant ($P = 0.12$). The overall sensitivity of the SDHO MTB test was only 20.6% (17 of 68), which is much lower than that of

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TABLE 1. Performances of microscopy examination and the SDHO MTB test with culture-confirmed PTB patients and non-PTB patients in Bangui, Central African Republic

Diagnostic test	No. of samples					% (95% confidence interval)				
	Total	True positive	False positive	True negative	False negative	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
Microscopy	99	55	0	31	13	80.9 (69.2–89.0)	100.0 (83.3–100.0)	100.0 (91.9–100.0)	70.5 (54.6–82.8)	86.9 (78.6–92.8)
SDHO MTB	99	14	3	28	54	20.6 (12.1–32.5)	90.3 (73.1–97.5)	82.4 (55.8–95.3)	34.1 (24.3–45.5)	42.4 (32.5–52.8)
<i>P</i>						<0.00001	NS ^a	ND ^b	<0.0001	<0.00001

^a NS, not significant.

^b ND, not determined.

sputum smear examination (80.9%; 55 of 68). The specificities of sputum smear examination (100.0%) and the SDHO MTB test (90.3%) were similar (Table 1).

This preliminary study indicates that the SDHO MTB test performed poorly compared to sputum smear examination in the detection of PTB. Similarly poor performance has previously been reported for other serological tests to identify PTB patients; in particular, sensitivity is poor to moderate (16% to 57%) for seven serological tests, including two immunochromatographic tests (ICT Tuberculosis and RAPID TEST TB) and five enzyme-linked immunosorbent assays (TUBERCULOSIS IgA enzyme immunoassay, PATHOZYME-TB complex, PATHOZYME-MYCO IgG, PATHOZYME-MYCO IgA, and PATHOZYME-MYCO IgM) (10). The same conclusion was also drawn more recently after evaluation in Botswana of a new prototype immunochromatographic strip and five commercially available serodiagnostic TB tests with a predominantly HIV-infected population of hospitalized patients with cough (12).

The sensitivity of sputum smear examination was much lower among HIV-positive patients than among HIV-negative patients. This is consistent with previous reports (9), and although the reasons are unclear, it could be due in part to the degree of cellular immunocompromise. The likelihood of a positive sputum smear is lower, because inflammation in the lung decreased with the severity of cellular immunocompromise associated with HIV. The same trend was observed with the SDHO MTB test, and this is not surprising because serological tests are not very sensitive in HIV patients (2). However, these results should not preclude further experiments using other commercial serological tests with large groups of TB- and HIV-positive patients to address the observation of low sensitivity.

Despite an acceptable specificity, this novel serological test lacks the sensitivity required to replace the sputum smear microscopy method in our population. Further improvements are needed before this test could be useful in our setting.

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