TB DIAGNOSTICS I

PC-100495-13   Poor correlation of smear microscopy for TB culture on solid and in liquid media during TB treatment

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Background: Sputum culture is considered the gold standard for diagnosing TB and monitoring treatment but it is often unavailable in resource-poor settings. Therefore, many national TB programmes base management decisions on smear microscopy performed during treatment.
Objective: This study investigates the relationship between smear microscopy and culture during TB treatment.
Methods: We analysed mycobacteriological results of serial sputum samples, submitted weekly for 8 weeks and monthly thereafter, during the first 17 weeks of TB treatment from 447 patients enrolled in the treatment-shortening REMox study. Patients were adults with smear-positive pulmonary TB, HIV-negative or HIV-positive with CD4 > 250 cells/μL, and received standard TB treatment or a 4 month regimen in which moxifloxacin replaced either isoniazid or ethambutol. Samples were processed for smear microscopy by Ziehl-Neelsen staining and for culture in both solid Löwenstein-Jensen (LJ) and liquid MGIT (mycobacterial-growth-in-tube) media. Predicted probabilities and odds ratios were calculated using mixed effects logistic regression.
Results: 6496 samples were analysed. Paired smear and LJ-culture data were available for 4422 samples. 4681 samples had paired smear and MGIT-culture results. The probability of a positive culture at week 8 given a positive smear was 0.75 on MGIT and 0.12 on LJ. The odds ratio reflecting the association between the culture result and the smear result was high but had very wide confidence intervals and decreased with time (Table). Similar relationships were observed for quantitative smear results. These results did not differ by HIV status.
Conclusion: Smear microscopy is a poor predictor of solid and liquid culture results during TB treatment, and the strength of the association decreases with time over the course of treatment. This may have implications for national programmes advising treatment decisions based on smear microscopy.

Table The predictive probability (PP) with 95% confidence interval of a positive culture on LJ or MGIT at weeks 0 to 17 visits given the smear result at that visit

Visit Week	Smear negative		Smear positive		Odds ratio (95%CI)
	PP	95%CI	PP	95% CI	
LJ					
4	0.24	(0.15–0.38)	0.85	(0.76–0.90)	10.1 (4.9–20.7)
8	0.01	(0.01–0.04)	0.12	(0.06–0.23)	7.2 (3.9–13.2)
12	0.00	(0.00–0.01)	0.05	(0.02–0.13)	4.0 (1.9–8.4)
17	0.01	(0.00–0.03)	0.08	(0.02–0.30)	2.9 (1.1–7.8)
MGIT					
4	0.69	(0.59–0.77)	0.96	(0.92–0.98)	17.1 (7.6–38.7)
8	0.30	(0.23–0.37)	0.75	(0.64–0.84)	9.2 (2.9–29.6)
12	0.10	(0.07–0.14)	0.30	(0.19–0.45)	38.3 (3.9–370.7)
17	0.09	(0.06–0.13)	0.21	(0.10–0.40)	8.5 (1.4–50.9)

PC-100042-13   Operational effectiveness of TB culture and drug susceptibility testing in a high-prevalence setting

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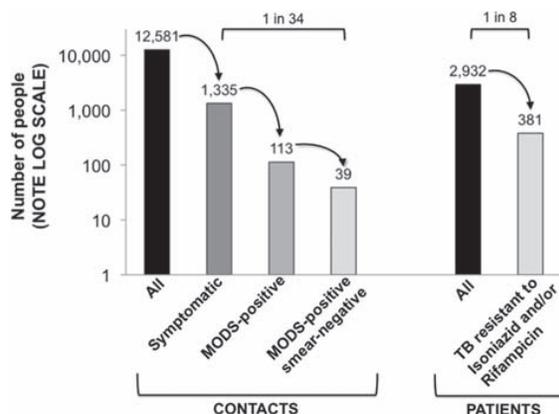e-mail: schumacher.samuel@gmail.com

Background: Liquid culture systems are available for TB testing that provide higher sensitivity than Ziehl-Neelson (ZN) microscopy and allow rapid concurrent testing for drug-resistance. Their scale-up is recommended in low- and middle-income countries but data on their effectiveness under operational conditions is scant.
Setting: Shantytown with 500 000-person population in Northern Lima, Peru that principally utilized ZN microscopy for TB diagnosis from 2002–2010.
Methods: The high number of TB suspects (>100 daily) did not allow culture testing of every sample therefore culture was focused on two high-risk groups: TB patients and their symptomatic contacts. 4267 Microscopic-Observation Drug-Susceptibility (MODS) cultures were performed for TB detection and concurrent drug-resistance testing.

Results: MODS testing of 2932 TB patients determined that 381 (13%) had drug-resistant TB (DRTB; i.e. resistant to isoniazid, rifampicin or both), so 7.7 patients needed to have MODS culture per drug-resistant case identified (16 per MDR case). Drug resistance was more common among re-treatment cases (26%; risk ratio = 1.9, $P < 0.001$; population attributable fraction: 16%). Thus, restricting MODS testing to the 22% of TB patients who were re-treatment cases would only detect 35% of all DRTB (39% of MDR-TB). Additionally among 12 581 contacts, 1335 (11%) had respiratory symptoms, 113 of whom were MODS culture positive (i.e., 0.9% of all contacts and 8.5% of symptomatic contacts). Of these culture-positive contacts 39 (35%) were ZN microscopy-negative. Thus 34 symptomatic household contacts needed to have MODS culture per smear-negative TB case identified.

Conclusion: In operational settings, modern diagnostic tests that offer sensitive diagnosis and rapid DRTB testing may provide greatest public health impact when focused on TB patients rather than on enhanced case-finding. These calculations may be adjusted for settings with different rates of smear-negative TB and DRTB.

PC-101296-13   A simple colour test for diagnosing MDR-TB and XDR-TB under field conditions

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Background: Increasing rates of drug-resistant and smear-negative TB require improved TB diagnostics that are easy to use, affordable and equipment-minimal. The MDR/XDR-TB Colour Test is a simple, Thin-Layer-Agar-based non-proprietary culture technique that offers concurrent MDR testing and XDR screening. We compared its performance with a standard culture technique.

Methods: Sputum samples were collected from patients with suspected TB ($n = 788$). Smear microscopy was done directly from sputum samples, which subsequently underwent culture with the Peruvian standard protocol of modified-Petroff NaOH-decontamination and culture on Ogawa medium. Samples for the Colour Test were collected in parallel directly into sputum pots containing disinfectant that decontaminated the sputum in-transit. Upon arrival in the lab, these were directly applied to selective culture medium without any processing. Positive cultures were indicated by colour change.

Results: 265 samples had a culture-positive result and
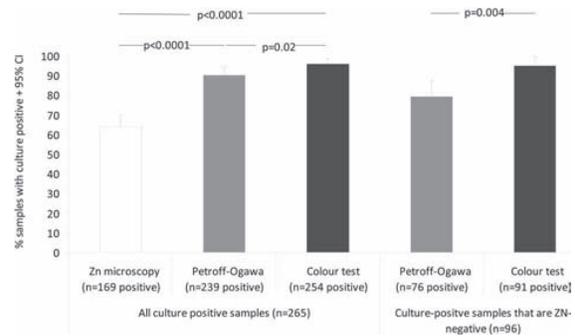
both Colour Test and Petroff-Ogawa were significantly more sensitive than ZN microscopy (96% and 90% vs. 63%; $P < 0.0001$). The Colour Test also had higher sensitivity than Petroff-Ogawa ($P = 0.02$) and this difference was greatest in the 128 smear-negative samples that were culture-positive (95% vs. 79%; $P = 0.002$). Results were obtained more rapidly in the Colour Test (17 vs. 21 days; $P < 0.0001$) with similar contamination rates (3.5% vs. 2.4%; $P = 0.2$). The Colour Test detected drug-resistant TB in 18% of all culture-positive samples the same day as culture detection with 99% agreement with delayed indirect testing.

Conclusion: The Colour Test is a simple culture technique that offers superior characteristics over the current standard culture method. It addresses the rising challenges of paucibacillary disease and drug-resistance while using simple and effective technology that is appropriate to resource-poor settings where these problems are most common.

PC-100618-13   Rapid direct MDR-TB testing better predicts clinical outcome than conventional delayed testing

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Background: Drug susceptibility testing (DST) is an important tool in the control of multidrug-resistant tuberculosis (MDR-TB). Conventional DST is done indirectly after first culturing the TB strain, thereby delaying the DST result. New DST tests are emerging that culture TB directly on antibiotic-containing media concurrently with drug-free culture. This leads to a much more rapid DST result, which may have an important positive impact on the patient's clinical outcome. Direct and indirect DST may have discrepant results and we therefore investigated the clinical