

FIND Scientific Forum on Recent Advances in TB Diagnostics

17 October 2008, 08:30-12:30
Havane Room, Palais des Congrès, Paris



Partnering for better diagnosis for all



FIND has recently celebrated its 5th birthday. During the FIND Scientific Forum that will be held in Paris in conjunction with the 39th Union Conference on Lung Health, FIND staff and partners will provide a broad overview of progress on TB diagnostics.

Agenda

Chair: Dr. Giorgio Roscigno, FIND
Co-Chair: Dr. Rick O'Brien, FIND

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| <p>8:30
FIND at five: an overview of FIND and its record.
<i>Dr. Giorgio Roscigno, FIND</i></p> | <p>10:35
Simplifying culture-based TB/MDR-TB testing for peripheral labs.
<i>Dr. Carlton Evans, Universidad Peruana Cayetano Heredia</i></p> |
| <p>8:50
Global efforts to control the MDR/XDR TB crisis.
<i>Dr. Paul Nunn, WHO</i></p> | <p>10:50
Point-of-care tests for TB: how close are we?
<i>Dr. Gerd Michel, FIND, and Dr. Marila Gennaro, UMDNJ</i></p> |
| <p>9:05
The role of UNITAID in support to the fight against MDR/XDR TB.
<i>Dr. Jorge Bermudez, UNITAID</i></p> | <p>11:20
IGRAs for the diagnosis of LTBI: are they relevant in TB endemic settings?
<i>Dr. Madhukar Pai, McGill University</i></p> |
| <p>9:20
The FIND TB diagnostic test portfolio: does it address the need?
<i>Dr. Mark Perkins, FIND</i></p> | <p>11:35
FIND demonstration studies: costing analyses, impact, and equity.
<i>Dr. Heather Alexander-Konopka, CDC/FIND, Mr. Hojoon Sohn, FIND, and Dr. Delia Boccia, FIND</i></p> |
| <p>9:40
FIND TB trials infrastructure and management.
<i>Dr. Catharina Boehme, FIND</i></p> | <p>12:05
Beyond policy to implementation: FIND activities in laboratory strengthening.
<i>Dr. C.N. Paramasivan, FIND</i></p> |
| <p>9:55
Rapid molecular diagnosis of M/XDR TB: LPA and beyond.
<i>Dr. Heidi Albert, FIND</i></p> | <p>12:20
Conclusion.
<i>Dr. Giorgio Roscigno, FIND</i></p> |
| <p>10:10
Coffee break.</p> | |

Simplifying culture-based TB/MDR-TB testing for peripheral labs

Carlton Evans, Universidad Peruana Cayetano Heredia

Background. The complexity and biohazard of conventional procedures for sputum liquefaction and decontamination largely restrict the use of TB culture with drug-susceptibility testing to reference laboratories. The complexity, advanced human capacity and expense of setting up and maintaining reference laboratories makes them a rare resource in the regions where tuberculosis is most common. Thus sensitive TB, MDR-TB and XDR-TB diagnostics are infrequently available to patients in resource-poor settings who have greatest need for them.

Objective. We aimed to optimize safe sputum processing and culture for TB diagnosis and drug susceptibility testing for basic field laboratories in resource-poor settings.

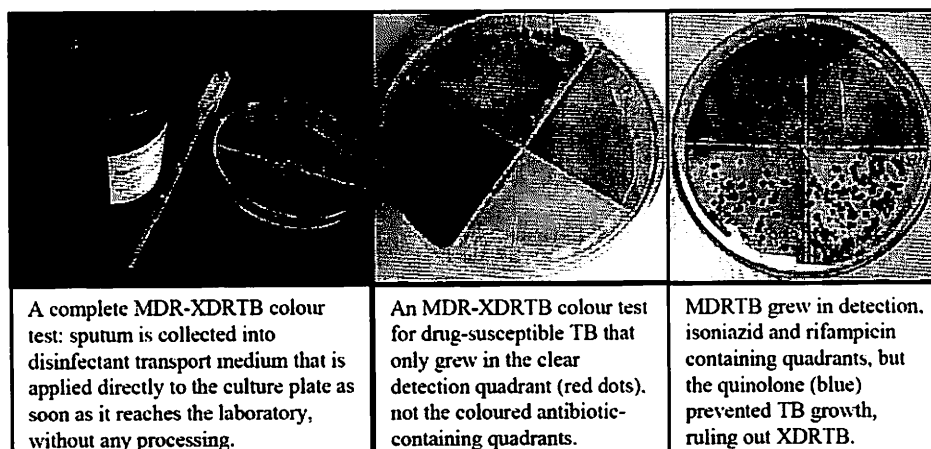
Strategy. In order to allow sensitive yet biosecure TB diagnostics in basic, regional laboratories we combined and refined a variety of sputum processing, culture, direct drug-susceptibility testing and tuberculosis detection techniques described by numerous researchers over the past several decades.

Participants. Patients with suspected pulmonary TB expectorated 385 sputa into pots containing disinfectant transport medium that liquefied and decontaminated sputum during transit. The sputum samples took between 6 hours and 5 days at room temperature to reach the laboratory.

Novel Colour Test technique. On arrival in the laboratory, the contents of the sputum pot were applied directly without any processing to each quadrant of a culture plate. The culture plate contained a transparent thin-layer of 7H11 agar made selective with antimicrobials to prevent contamination and also incorporated a colour-change indicator to detect positive cultures. Direct drug susceptibility testing for isoniazid, rifampicin and ciprofloxacin was also carried out concurrently in the other quadrants of the same culture plate. Immediately after sputum application, the culture plates were closed, double-sealed and incubated. Positive cultures were identified by naked-eye examination for colour change and *M. tuberculosis* was further confirmed by examining the areas of colour change within the sealed plates under a normal microscope with a low-power 4x objective.

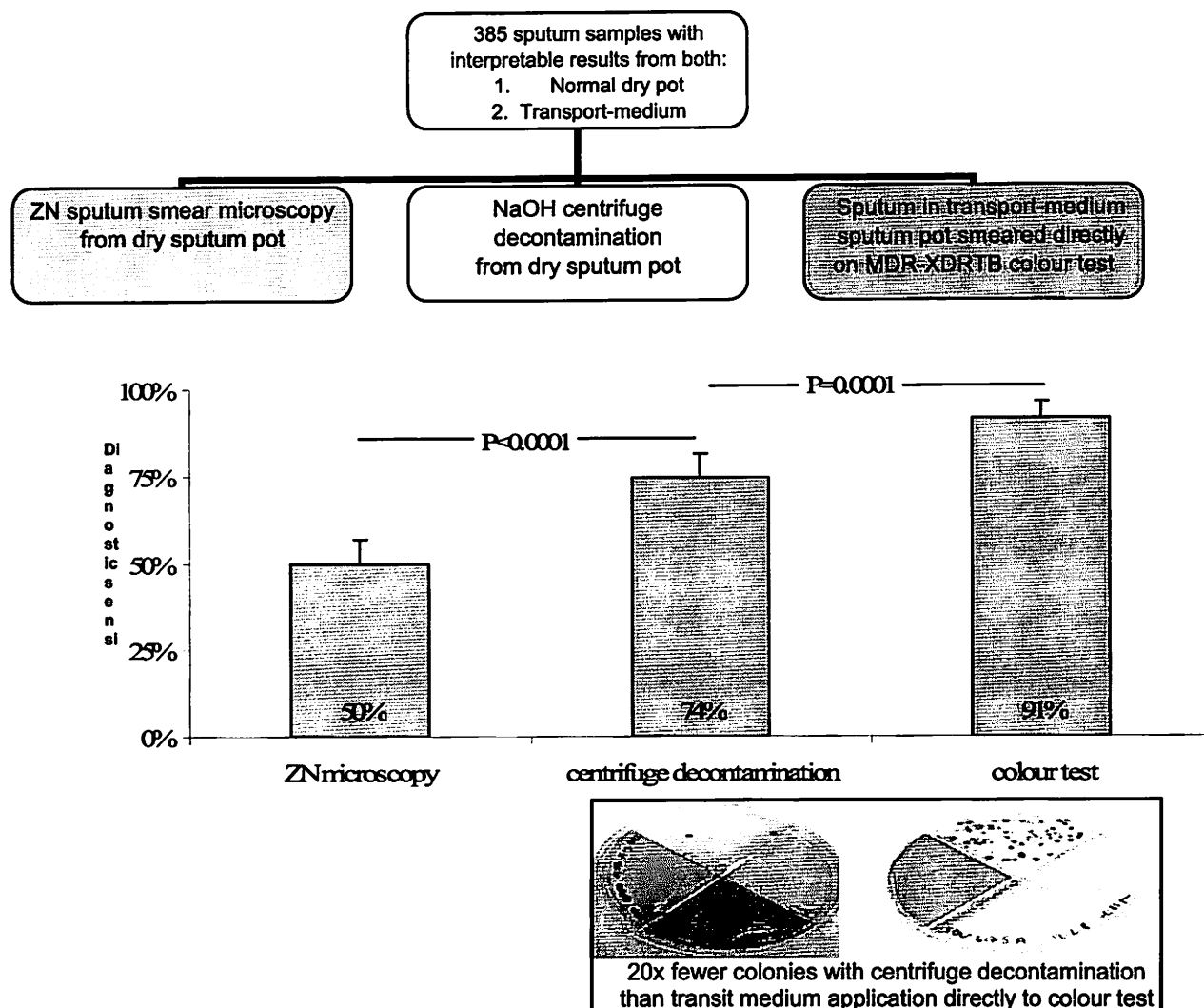
Control testing. For comparison, the same patients expectorated another sputum sample into a normal dry pot that was processed by the gold-standard Centres for Disease Control reference laboratory technique utilising N-acetyl L-cysteine NaOH decontamination with centrifugation, vortex re-suspension and culture on 7H11 agar.

Results. For 385 sputum samples cultured by both methods, 149 were culture-positive for *M. tuberculosis* by one or both methods, 49% of which were also smear microscopy positive. The gold standard test was culture-positivity by either test. The sensitivity of the novel test was 91%, significantly more sensitive than the conventional centrifuge decontamination method (74% diagnostic sensitivity, $p=0.0001$) and yielded significantly more tuberculosis colonies ($p<0.0001$). The median estimated time to culture positivity with concurrent drug-susceptibility testing was 16 days, slightly faster than the centrifuge-decontamination method ($p<0.01$). Contamination resulted in the loss of 3.6% and 1.0% of test results, respectively ($p=0.02$).



Feasibility. Processing 30 fresh sputa with the novel test took less than an hour, required less training and involved a similar sample processing bio-hazard to sputum smear microscopy, after which cultures were permanently sealed. In contrast, standard centrifuge decontamination took several hours, required specialized skills and risked biohazardous aerosol formation. The colour test materials cost ~\$1 and utilized standard laboratory equipment (a normal incubator and a conventional microscope).

Conclusions. This simple colour-change technique allowed safe, inexpensive and sensitive TB diagnosis with concurrent testing for MDRTB and screening for XDRTB in basic field-level laboratories. This has the potential to make modern TB diagnostics more widely accessible in resource-poor settings to increase equity in TB diagnosis.



The collaborative work described here was carried out by Beatriz Herrera^{1,2}, Eric Ramos¹, Robert H. Gilman^{1,2,3}, Louis Grandjean², Laura Martin², Jessica Alvarado^{1,2}, Teresa Valencia^{1,2}, Willi Quino¹, Gurjinder Sandhu^{1,2}, Jessica Alva^{1,2}, Rosario Sosa^{1,2}, Silvia Carrera^{1,2}, David Coleman⁴, Denis Mitchison⁴, Carlton A. Evans^{1,2,3,5}
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