CORRESPONDENCE

MODS Assay for the Diagnosis of TB

TO THE EDITOR: In their article on the use of microscopic-observation drug-susceptibility (MODS) culture for the diagnosis and direct detection of multidrug-resistant tuberculosis, Moore et al. (Oct. 12 issue)[1] state that MODS culture offers faster and more sensitive results than existing gold-standard methods. This study is one of the few performed in a target population with a rather simple and inexpensive method that seems to be appropriate for countries with limited resources.

However, we would like to stress that there are other options that have recently been described[2] and are currently under evaluation. As compared with MODS culture, the nitrate reduction assay, based on a simple procedure involving the use of Löwenstein–Jensen medium, has been tested in sputum samples with similarly good results.[3] The thin-layer agar method, which is similar to MODS culture but with solid medium and standard microscopes, had better results than conventional methods when evaluated in target populations.[4] In ongoing evaluations, the thin-layer agar method has also outperformed the reference method for detecting multidrug-resistant tuberculosis. In addition, direct colorimetric methods with redox indicators have performed very well[5] and are under further evaluation. A disadvantage of the MODS method remains the requirement of an inverted microscope, which is not routinely available in laboratories that perform diagnostic tests for tuberculosis.

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TO THE EDITOR: The MODS assay has certain limitations. Microscopical differentiation between microcolonies of *Mycobacterium tuberculosis* and those of rapidly growing mycobacteria may be difficult. The assay requires daily examination, is time-consuming, and as highlighted by Iseman and Heifets,[1] carries a risk of laboratory transmission. We therefore agree that the microscopical-observation method, although promising, will require modification and adaptation before it can be recommended for widespread use.

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THIS WEEK'S LETTERS

THE AUTHORS REPLY: Although there is merit in the alternative methods Palomino and colleagues mention, elements of which gave rise to the MODS assay, the culture time for the Löwenstein–Jensen–based nitrate reduction assay is three to four times that for the MODS assay, with lower sensitivity, and as with the direct colorimetric assay, data for smear-negative samples are lacking. Unlike MODS culture, both techniques involve the potentially hazardous opening of mature tuberculosis cultures to add a specific reagent. The thin-layer agar method is rapid, but its sensitivity is usually lower and its contamination rate higher than those of the Löwenstein–Jensen method, and no data on drug-susceptibility testing have been published.

In our opinion, MODS culture is actually safer than any indirect drug-susceptibility testing method, since culture amplification and direct drug-susceptibility testing occur within a closed system: the MODS plate is inoculated and then sealed within a ziplock bag. It is not manipulated again, since all readings, including those for drug-susceptibility testing, are done through the bag. The handling of cultured *M. tuberculosis* at bacterial concentrations thousands of times those of clinical specimens, which is required for secondary drug-susceptibility testing, dwarfs the biohazard risk associated with sputum-decontamination processes common to all culture methods. This handling risk is entirely avoided with the MODS assay.

Hasan and Irfan did not use ziplock bags, because this important detail was omitted from previous articles on the MODS assay.[1-3] We do not believe that a MODS laboratory needs to meet biosafety level 3 standards. Combining the use by laboratory staff of respirators approved by the National Institute for Occupational Safety and Health and appropriate protective clothing with a well-positioned, properly maintained class II biologic safety cabinet that recirculates exhausted air through a high-efficiency particulate air (HEPA) filter into a closed room, should be adequate. With respect to rapidly growing mycobacteria, these organisms should overgrow MODS plates by day 5, a phenomenon not seen with *M. tuberculosis.*

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Refining Prognosis in Non–Small-Cell Lung Cancer

TO THE EDITOR: Potti et al. (Aug. 10 issue)[1] apply a metagene model to the profiling of non–small-cell lung cancer (NSCLC) and demonstrate superior performance in predicting tumor recurrence and survival, as compared with a clinical model. We believe that the impressively contrasting results could be partially due to the incompleteness of the clinical model the authors used. Classifying NSCLC into squamous-cell carcinoma and adenocarcinoma has not been predictive for prognosis in general. However, subtypes of adenocarcinoma — bronchioloalveolar carcinoma and mixed adenocarcinoma with a bronchioloalveolar component, which account for approximately 20% of cases of early-stage NSCLC — have a much better prognosis than do other subtypes.[2] Potti et al. did not consider these adenocarcinoma subtypes.

In addition, the literature[3] and our recent work demonstrate that the histologic grade is a significant predictor of both tumor recurrence and survival,[4] and there is a high correlation between histologic features and gene-expression profiles.[5] Our work also shows that incorporating the adenocarcinoma subtype and histologic grade into clinical models would provide a prediction very similar to that of a well-validated, 50-gene panel for survival.[5]

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