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**VALIDATION OF THE MICROSCOPIC-OBSERVATION  
DRUG-SUSCEPTIBILITY (MODS) TECHNIQUE FOR DRUG-  
SUSCEPTIBILITY TESTING DURING TUBERCULOSIS THERAPY**

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The Microscopic-Observation Drug-Susceptibility (MODS) technique has proven reliability for diagnosis and concurrent direct isoniazid and rifampicin drug-susceptibility testing for patients with suspected tuberculosis (TB). However, MODS has not been validated during TB treatment, when misleading mycobacterial sub-populations may be selected and when antimicrobials in sputum may confound *in vitro* direct drug-susceptibility testing. Consequently, patients whose sputum was collected after treatment commenced (or whose pre-treatment MODS assay failed) miss the opportunity for a rapid MODS drug-susceptibility test. We therefore assessed MODS reliability during TB treatment. Sputum samples were collected from the same patients both prior to and during TB treatment. Sputa were tested with the MODS technique that provided direct concurrent isoniazid and rifampicin drug-susceptibility testing. Subsequently, the sub-cultured TB strain was tested with conventional indirect drug-susceptibility testing with the alamar blue and tetrazolium microplate assays. Results of these direct and indirect tests were compared with reference to the patients' phase of conventional first-line treatment. Paired direct MODS and indirect drug-susceptibility results were available for 1552 samples, 928 in the month prior to treatment, and 624 during therapy. TB therapy had no effect on the accuracy of direct drug-susceptibility testing relative to indirect testing. Specifically, the agreement between direct and indirect testing, respectively, was 92% vs. 91% for isoniazid susceptibility; 97% vs. 97% for rifampicin susceptibility; and 97% vs. 96% for MDRTB testing (all  $P > 0.1$ ). Treatment duration also had no effect on the level of agreement ( $P > 0.1$ ). In conclusion, these results validate MODS drug-susceptibility testing during treatment. Thus, patients who have commenced TB therapy may be offered rapid drug-susceptibility testing with the MODS technique.