Editorials

A step forward in the evidence-based treatment of opportunist mycobacteria

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While the treatment of *Mycobacterium tuberculosis* is firmly based on multiple controlled clinical trials in various settings^{1,2} and meet the criteria for 'A' category recommendations,³ the management of opportunist mycobacteria (mycobacteria other than tuberculosis (MOTT), non-tuberculous mycobacteria, environmental mycobacteria, atypical mycobacteria) is much less so. When the Joint Tuberculosis Committee of the British Thoracic Society reviewed the evidence base for the treatment of this group of organisms in HIV negative persons for their 2000 treatment guidelines,⁴ only the treatment recommended for *M. kansasii* was based on a prospective controlled study.⁵ The treatment recommendations for the other common opportunist mycobacteria causing respiratory disease in HIV negative persons, usually secondary to underlying chronic obstructive pulmonary disease (COPD) or structural lung disease—*M. malmoense*, *M. avium intracellulare*, and *M. xenopi*—were largely based on retrospective non-controlled studies.^{6–11}

One of the other difficulties with treatment in opportunist mycobacteria is the fact that, unlike with *M. tuberculosis* where the drug susceptibility data have to be scrupulously followed,¹ the drug susceptibility data using in vitro testing may not correlate at all with the clinical response to treatment. Studies have shown synergy between rifampicin and ethambutol and for other drugs in opportunist mycobacteria which had been reported as resistant to these drugs individually on in vitro testing.^{12–14}

The results of the first randomised trial of regimens of rifampicin and ethambutol with or without isoniazid reported in this issue of *Thorax*¹⁵ give a basis on which treatment recommendations can be made, but also raises further questions. The results of the two reported regimens are as good as those using 5–6 drugs and much better tolerated.^{6–11} They also confirm that drug susceptibility tests using the standard modal resistance technique¹⁶ do not predict clinical or bacteriological response. There are some differences between the regimens and the organisms depending on which end point is selected. Although for individual organisms fewer deaths occurred with the rifampicin/ethambutol regimen, this only reached significance when the results for all three organisms were combined. Using the outcome variable of treatment failure/relapse, the rifampicin/isoniazid/ethambutol combination is superior, particularly for *M. avium intracellulare*. The "bottom line" message appears to be that rifampicin/ethambutol are best for *M. malmoense* and *M. xenopi*; because of the possibility of higher mortality, the addition of isoniazid should be reserved for *M. avium intracellulare* which has failed to become culture negative.

While giving data from which to consider treatment recommendations, the study also shows relapse/failure rates

of 10–28%, outcomes which are much worse than for *M. tuberculosis*. Better regimens are needed and the results of the ongoing study using macrolides or quinolones as well as rifampicin/ethambutol will be eagerly awaited to see if these give better outcomes. The authors also raise the question as to whether individual drug susceptibility data should be given when these opportunist mycobacteria are isolated because of the lack of correlation with clinical outcome, and wonder whether either no data or only data concerning susceptibility to drug combinations should be reported. The feasibility of the latter suggestion would need discussion with the United Kingdom Mycobacterium reference centres and units and results in terms of prediction of outcome would need to be validated.

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