Susceptibility of a series of routine sputum samples for antituberculosis chemotherapy in Gweru, Zimbabwe

To the Editor: Resistance of *Mycobacterium tuberculosis* to the commonly used antibiotics in national tuberculosis programmes (NTPs) is a growing concern in many parts of the world.[1] Nevertheless there is much anecdotal, but little published, evidence that drug resistance is becoming an important barrier to effective TB control.[2] In Zimbabwe the only routine source of data on drug resistance that is going further than individual case management is that of the national TB reference laboratory. This institute is performing routine drug susceptibility testing on sputum samples for the whole country. According to the NTBP guidelines, this test is only done on specific indications, i.e. when a sputum-positive patient has not converted to negative after 2 months of intensive antituberculosis chemotherapy.[3]

To get an idea of the prevalence of single drug resistance, we performed susceptibility testing on a sample of 134 consecutive TB culture-positive patients, diagnosed between September 2000 and September 2001 at Gweru Provincial Hospital. These patients were selected for a study that examined the characteristics of different laboratory methods, and the accuracy of the diagnosis in routine circumstances. The results are described elsewhere;[4] this letter focuses on the susceptibility testing.

Two samples (1.5%) were resistant to isoniazid and streptomycin, 2 were resistant to streptomycin only, and 1 (0.7%) was resistant to ethambutol only. None of these patients had received TB treatment before, they converted when sputum was checked after 2 months, and they were cured after the continuation phase. There were 4 men and 1 woman. No resistance to rifampicin was detected. Among the 134 patients, 7 (5.2%) had taken TB drugs before, be it a complete course (5 'relapses'), or a partial course (2 'defaulters'). TB cultures of these patients were fully sensitive to the tested drugs. Quality control of the resistant samples was provided by the Department of Medical Biochemistry of Stellenbosch University, South Africa. All resistant samples detected in this study were double checked using the minimal inhibitory concentration method for isoniazid and rifampicin resistance. The RpoB gene (linked to rifampicin resistance) and the KatG gene (linked to isoniazid resistance) were sequenced to look for genomic mutations. A mutation in the KatG gene codon 315 was detected in only 1 isoniazid-resistant sample, suggesting that the resistance of the second isoniazid-resistant sample was associated with mutations in other genes.

Drug resistance testing has been recommended by the World Health Organisation (WHO) for monitoring and guiding TB treatment programmes. Initial or acquired resistance is considered a key indicator for programme performance. Resistance is seen as a man-made problem, resulting from inadequate treatment regimens or poor compliance. The results of this study are reassuring in the sense that no case of multi-drug resistance (MDR) was detected among this series of patients, neither clinically nor microbiologically. The levels of initial resistance are far below the arbitrary threshold of 5% that is considered the cut-off point to question treatment regimens. No single-drug resistance was detected among relapse cases and no resistance in particular was detected against rifampicin, the most important drug to prevent failures or relapses. These results suggest that the TB programme was performing well at the time of the study and that the risk of developing a problem of MDR with public health implications is still low in this province.

It must be made clear, however, that this sample was not, and was not meant to be, representative of the whole country. It is recommended that a resistance surveillance programme be set up covering the whole country, based on randomised sampling techniques as described by the WHO. This would give a more accurate idea of resistance patterns throughout the country, and if done on a regular basis, on trends over time. Indirectly, it would also be a tool to monitor the NTBP performance. As MDR strains are inevitably preceded by single-drug resistant strains, monitoring of the latter could provide vital information on the risk of developing MDR in this community.

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1. Kochi A, Vareldzis B, Styblo K. Multi-drug resistant tuberculosis and its control. *Res Microbiol* 1993; 144: 104-110.
2. World Health Organisation. *Guidelines for surveillance of drug resistance in tuberculosis.* Tuberculosis programme, World Health Organisation, Geneva and International Union Against Tuberculosis and Lung Diseases, Paris, 1994. WHO/TB/94.178
3. Ministry of Health and Child Welfare Zimbabwe. *Zimbabwe Tuberculosis Control Programme Manual.* 2nd ed. Harare: Ministry of Health and Child Welfare, Epidemiology and Disease Control, 1999.
4. Apers L, Mutsvangwa J, Magwenzi J, *et al.* A comparison of direct microscopy, the concentration method and the mycobacterium growth indicator tube for the examination of sputum for acid-fast bacilli. *Int J Tuberc Lung Dis* 2003; 7: 376-381.