patients had high mycobacterial load in sputum samples. Such patients had poor prognostic characteristics and worse outcomes.

In patients with very advanced immunodeficiency, pulmonary radiographic abnormalities are not a good index of mycobacterial load. Indeed, one third of patients in this clinical setting with sputum culture-positive tuberculosis have normal chest radiographs [2, 3]. Minor differences in radiographic extent of disease therefore did not reach statistical significance when comparing those with Xpert-positive and Xpert-negative disease [1].

That mycobacterial sputum load was higher in those with lower CD4 counts was supported by median times to positivity (TTP) in culture. In those with CD4 counts <150 cells/µL the median TTP was 15 days (interquartile range [IQR], 11–21) compared to 19 days (IQR, 14–23) among those with CD4 counts ≥150 cells/µL. Further, strong evidence of a higher mycobacterial load in those with lower CD4 cell counts in this cohort is provided by more frequent detection of mycobacterial antigen lipoprotein and of Mycobacterium tuberculosis in urine samples [4, 5]. These data collectively indicate that in very advanced immunodeficiency, high mycobacterial load does not remain compartmentalized within the lungs but is frequently disseminated.

Theron and colleagues inappropriately question the statistical association between Xpert results and CD4 counts [1]. Strong statistical associations were observed in both unadjusted and fully adjusted analyses. That strong associations were found indicates that the sample size (n = 89) was not too small. In our paper we drew conclusions that were logically plausible. We believe the Xpert MTB/RIF assay has great potential to expedite diagnosis and improve survival [7].

Notes

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1. Lawn SD, Kerkhoff AD, Vogt M, Ghebrekris- tos Y, Whitelaw A, Wood R. Characteristics and early outcomes of patients with Xpert-negative disease [1]. Their study of just 46 HIV-infected patients does not show the inverse association but rather found no association between the sensitivity of Xpert MTB/RIF and CD4 count (16 of 21 patients with CD4 counts ≥200 cells/µL vs 15 of 23 patients with CD4 counts <200 cells/µL; P = .52). A larger study is therefore clearly warranted in this patient population.

Our findings suggesting that those patients with the most advanced immunodeficiency have higher mycobacterial load, more disseminated disease, a higher frequency of positive Xpert results, worse prognostic characteristics, and higher mortality rates are statistically robust and biologically plausible. We believe the Xpert MTB/RIF assay has great potential to expedite diagnosis and improve survival [7].

Reply to Theron et al

To the Editor—We thank Theron and colleagues for their interest in our work. It appears that they seek clarification regarding how the sensitivity of the Xpert MTB/RIF assay for human immunodeficiency virus (HIV)-associated pulmonary tuberculosis varies in relation to blood CD4 cell counts and also how this likely reflects mycobacterial load. They raise questions regarding the correlation of Xpert results with radiographic appearances and time to positivity of cultures, statistical analyses, sample size, and differences with regard to the findings of their own study.

In our study, patients with advanced HIV-associated immunodeficiency enrolling in an antiretroviral treatment (ART) service were intensively investigated for tuberculosis regardless of symptoms [1]. Among those with cultureConfirmed tuberculosis, we found a higher sensitivity of Xpert MTB/RIF among those with lower CD4 counts, suggesting that these


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